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Coöperation Is Influenced by Conditions That Obtain in All Divisions of Pharmacy and the Mutual Relationship of Those Engaged in Pharmacy Will Speak for It and Reflect Its Service.

Vol. XXVII, No. 4 APRIL, 1938

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 86th ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN MINNEAPOLIS, MINN., Hotel Nicollet, August 22–27, 1938.

The 1938 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Minneapolis, Minn.

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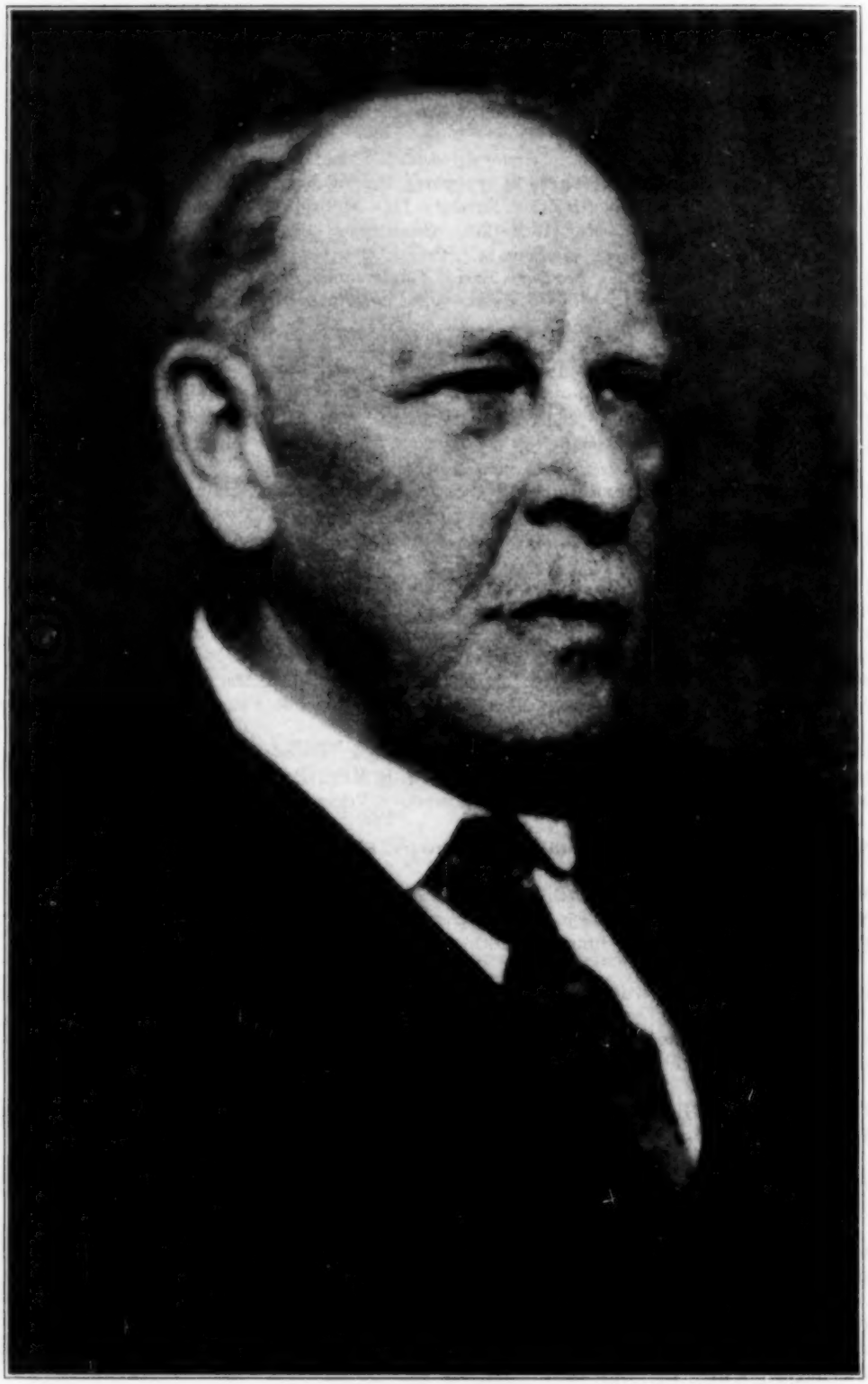

Courtesy of Dr. C. P. Wimmer.

HENRY HURD RUSBY.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXVII APRIL, 1938 No. 4

HENRY HURD RUSBY.

Dr. Henry Hurd Rusby was born in Franklin, N. J., April 26, 1855, the son of John and Abigail (Holmes) Rusby. He attended Massachusetts State Normal School, 1872–1874. He also attended the Centenary Collegiate Institute at Hackettstown, the next year he taught at a country school, and in 1882 he matriculated at the College of Physicians and Surgeons. He served as clinical clerk on the medical staff at a women's asylum on Blackwell Island. In 1876 he was awarded a medal at the Centennial Exhibition for an herbarium of plants of Essex County, New Jersey. As Assistant at the Smithsonian Institution he made botanical explorations through Arizona and New Mexico, of interest to medical botany; and explored South America, 1885–1887, crossing the continent.

He entered service with Parke, Davis & Co., which resulted in a continuation of botanical explorations and employment with the firm as botanist and pharmacognosist. In 1884 the anesthetic properties of cocaine were discovered and he was sent to Bolivia to investigate the plant and procure supplies of the leaves; he was sent to Chile to locate the Cheken plant and secure supplies; he learned of the medicinal uses of pichi.

From 1888–1930 he was Professor of Botany, Physiology and Materia Medica, Department of Pharmacy, Columbia University, and Dean of the Faculty; Professor, Materia Medica, U. and Bellevue Hospital Medical College, 1897–1902; Honorary Curator, Economic Museum, New York Botanical Garden (Chairman, Board of Scientific Directors, 1908–1917, and member of the Board of Managers); Revision Committee, 7th, 8th and 9th revisions, U. S. P.; member, Revision Committee of National Formulary; Chairman, Commission Pan-American Medical Congress for study of American medicinal flora; Honorary member, Pharmaceutical Society of Great Britain; Honorary member, Instituto Medico Nacional of Mexico; President, Torrey Botanical Club, 1905–1912; President, AMERICAN PHARMACEUTICAL ASSOCIATION, 1909–1910. Expert in drug products in Bureau of Chemistry, U. S. Department of Agriculture, 1907–1909; then pharmacognosist in same bureau, 1912–1917. Secured the vindication of Dr. Wiley and associates from charges, 1911. Author: "Essentials of Pharmacognosy," 1895; "Morphology

and Histology of Plants," 1899; "Materia Medica of Buck's Reference Handbook of the Medical Sciences (eight volumes)," 1899; "National Standard Dispensatory," 1905; "Wild Vegetable Foods of United States," 1906; "Fifty Years of Materia Medica," 1907; "Manual of Botany," 1911; "Three Hundred New Species of South American Plants;" "A Guide to the Economic Collections of the New York Botanical Garden;" "Properties and Uses of Drugs," 1930; "Jungle Memories," 1933. Has written much on medicinal botany and contributed many hundreds of new species and genera; introduced important drugs to American Materia Medica, among them, cocillana, mire and caapi. Awarded Hanbury Medal, British Pharmaceutical Association, 1929.

Additional contributions to the active life of Dr. Rusby may be found in the History of the College of Pharmacy of the City of New York by C. P. Wimmer, pages 267–277; the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION (December 1920), pages 1921–1932; various volumes of ASSOCIATION Proceedings; "Who's Who," which were drawn upon for data.

Dr. Rusby married Margaretta S. Hanna in 1887.

The Flückiger Medal will be awarded to Dr. Rusby in New York City, May 30th. See March JOURNAL.

PARTS OF ADDRESSES AND NOTES FROM THE VIRGINIA PHARMACEUTICAL SYMPOSIUM.

The Virginia Pharmaceutical Symposium was held in Richmond, February 18th, as a part of the Centennial of the Medical College of Virginia.

More than 125 delegates from all sections of the state were present. The sessions were held in the auditorium of the Richmond Academy of Medicine. The symposium ended with a luncheon given by the Medical College of Virginia at Cabaniss Hall for the delegates.

Chief speakers were Dr. I. C. Riggin, State Health Commissioner, Eldon Roberts, Jr., of Newport News, Virginia, and J. Leon Lascoff, New York, president-elect of the AMERICAN PHARMACEUTICAL ASSOCIATION.

Dr. Riggin spoke on "Opportunities of the Pharmacist as Health Educator," Mr. Roberts on "The Practice of Professional Pharmacy."

Dr. Riggin reviewed the growth of pharmacy in Virginia and discussed its relation to the profession of medicine and to public health. "A special service can be rendered in the venereal disease problem," he said. "Outside of the actual compounding of drugs, it is believed that the pharmacist's biggest public health opportunities are in the contact possibilities of his establishment."

President-Elect Lascoff urged the separation of pharmacy and drug store, stating it was not fair that a man with no pharmaceutical training should compete on the same terms with a man who has spent the best years of his life in study.

"In my opinion," he said, "as long as we have no ownership law, the boards of pharmacy have not the power to refuse anybody permission to open a drug store. I believe that the State Board of Pharmacy should have the power to regulate drug stores."

EDITORIAL

E. G. EBERLE, EDITOR 2215 Constitution Ave., WASHINGTON, D. C.

COÖRDINATION IN THE PHARMACY AND THE DRUG INDUSTRY.

THE OPPORTUNITIES which enable one druggist to select his own way of carrying on his business and another according to another plan which differed greatly within the law have been shaped by Boards, and the pharmaceutical education by Schools has advanced the practice of pharmacy. Here is an opportunity for coördination in bringing about a general improvement which will be for the benefit of all by the program which has been arranged.

A sincere effort is being made to strengthen and advance the status of the teaching practices in the institutions of pharmacy, so that "know thyself" may not only profit but point to further advancement and develop hope for better conditions in all divisions of pharmacy. Local and state pride will answer some of the questions of the investigation. It will bring greater financial support to institutions that should be encouraged by their citizenship, others may be disappointed in their efforts. Adequate education is of first importance; the welfare of the people is entitled to and expects efficient pharmaceutical service and herein is the basis of its educational system and the desire of its educators.

THE LIBRARY AND MUSEUM.

THE LIBRARY, the Laboratory and Research are closely related subjects. The importance is shown by the inspection being made on the activities of Schools of Pharmacy. Members of the Inspection Committee are asked to make notes with respect to the following: Training of the Librarian, the number of hours spent in the library, hours per day the library is open, the system followed in cataloging the books; approximate number of text and reference books pertaining to pharmacy, pharmaceutical chemistry, pharmacognosy, pharmacology, toxicology, therapeutics, materia medica, commercial economics, history of pharmacy, etc.

Herein is part of the service of the AMERICAN INSTITUTE OF PHARMACY, which will grow in value; it adds to that given by the other libraries of Washington. While smaller the library of the ASSOCIATION has been in position to aid those doing research work in the divisions of the drug industries of the Government and other laboratory activities and thus make this part of a great library system; this is added to by the Abstract Section of the JOURNAL and greatly by the Laboratory in the INSTITUTE OF PHARMACY.

Pharmacists cannot possess all the books and the information of a student must depend on what is made available for him. Work of bringing the publications into order is now proceeding and will gradually increase the reference value.

Dr. Charles Whitebread, of the Smithsonian Institution, stated several years ago that there were few historical collections in the United States. Pharmacy has had a long and honorable history and its record should be illustrated. Pharmacy's historical material is scattered about and, therefore, does little good. Individuals should permanently place the historical matter and records where they will be of general good; and there should be exchanges established between museums. There is a problem of keeping the collection in good state, and another of devising ways and means of illustrating the art of science, and industrial phases of pharmacy—is work which will test anyone's ingenuity.

SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins; H. M. Burlage, W. G. Crockett, E. V. Lynn, C. O. Lee, L. W. Rising, L. W. Rowe, Heber W. Youngken, Ralph E. Terry, Carl J. Klemme.

A QUANTITIVE STUDY OF THE TOXICITY AND EFFICIENCY OF PICROTOXIN.

BY RICHARD KOHN.*

Picrotoxin, known for a long time to the pharmacologist as an extremely potent drug, was considered too dangerous by the clinician for human use. It is a merit of Tatum and his co-workers (1, 2, 3) to have demonstrated in recent years that this drug represents an efficient respiratory stimulant and possesses a powerful analeptic action, especially against barbiturate depression, which makes it useful clinically. Koppanyi (4, 5) and others have extended this work experimentally and several favorable clinical reports have been published in the meantime (6, 7, 8), proving its usefulness in acute barbiturate poisoning.

At this time it seems desirable to report in brief our studies concerning the assay of Picrotoxin solutions for toxicity and efficiency and to give some data about stability and other properties of the solution.

Picrotoxin is not very soluble in water but a 0.3% solution is stable. Such a solution with addition of 0.5% chlorbutanol was used in all our experiments. The following investigations were conducted on rabbits. The average weight of the animals was 1.3 to 1.5 Kg.; albinos were used only in the first experiments but later discarded since they seem to be more sensitive than the colored races. The sex did not influence the results. All animals were kept in an air-conditioned building on a diet consisting of oats, alfalfa and water.

I—TOXICITY.

The determination of the lethal dose was conducted on 182 rabbits in a period of about twenty months. This gave an opportunity to compensate for an eventual fluctuation in the sensitivity of the animal material. All rabbits were injected intravenously. Table I gives the number of animals used on each dose and the number and percentage of death. Fifty-seven per cent of the rabbits injected with 1.0 mg./Kg.[1] showed one or more attacks of convulsions. Convul-

TABLE I.—TOXICITY OF PICROTOXIN IN RABBITS; INTRAVENOUS INJECTION.

No. of Animals.	Dose, Mg./Kg.	No. of Deaths.	Per Cent.
26	1.0	2	7.7
30	1.1	11	36.8
30	1.2	12	40.0
24	1.3	16	66.7
16	1.4	13	81.5
34	1.5	29	85.4
16	1.6	16	100.0

TABLE II.—DAILY INTRAMUSCULAR INJECTIONS OF PICROTOXIN.

Rabbit No.	Daily Dose, Mg./Kg.	Number of Days Given.	I. V. Dose Given Day after Last I. M. Injection.	Result.
682	1	7	1.5 mg./kg.	Death
623	1	7	" " "	"
577	1	7	" " "	"
598	1	10	" " "	"
578	1	10	" " "	"
596	1	10	" " "	"
441	1	13	" " "	"
603	1	7	" " "	Surv. (Died 1 day later with 1.6 mg.)

* Abbott Laboratories, North Chicago, Ill., Department of Pharmacology.

[1] Mg./Kg. = mg. per Kg. body weight.

sions occurred in all animals if 1.3 mg./Kg. was given. As it is well known, a period of several minutes elapses between the injection of the drug and the appearance of convulsions, but there is no strict relationship between the size of the dose in the range given on Table I and the latent period. Similarly, the time until death varied greatly from approximately fifteen minutes to two hours.

The results show a rather sharp increment in toxicity from 1.0 to 1.1 mg./Kg. and again from 1.2 to 1.3 mg./Kg. According to the rules of statistics a smoother curve would be obtained from an even larger number of animals. However, from the present results the M. L. D. for fifty per cent of the animals can be calculated as between 1.2 and 1.3 mg./Kg. As already mentioned these results represent the summary of experiments carried out at different times. Since we have found that there really exists a change in the sensitivity in different groups of animals we

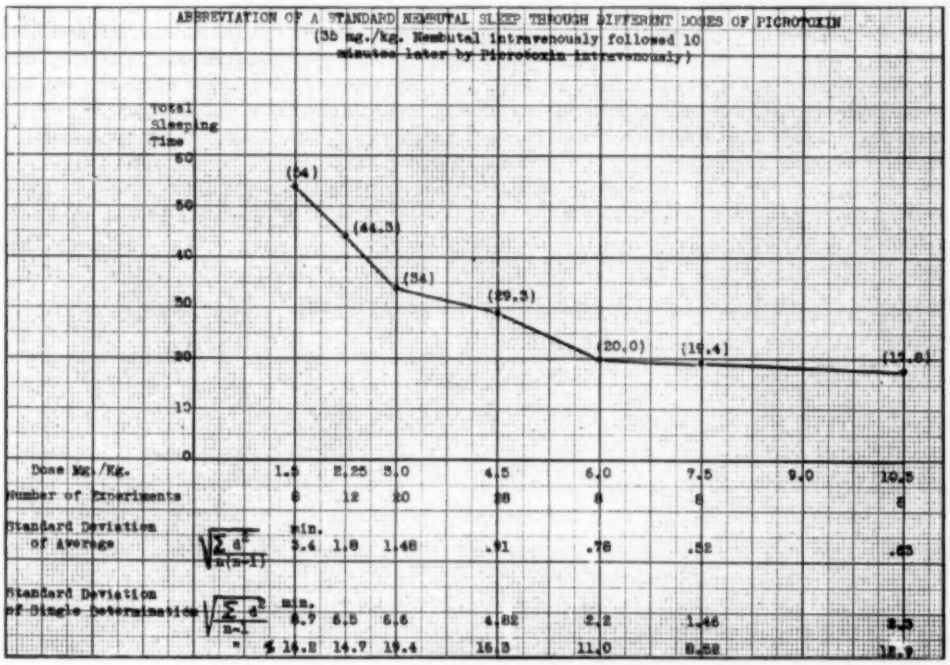

Fig. 1.

thought it practical to base the assay for toxicity upon the limits rather than upon the M. L. D. for fifty per cent. We define, therefore, a solution as of standard strength if of five rabbits (1.3 to 2.2 Kg. weight) injected with 1.0 mg. Kg. intravenously not more than one dies and not more than one survives of five animals injected with 1.5 mg./Kg. If the results do not check with this standard the experiment should be repeated with another set of animals.

II—TOLERANCE.

The older literature (9) gives very little information on the question whether or not a tolerance is formed by a continued administration of Picrotoxin. We have therefore injected a number of rabbits over a period of several days with a sub-lethal dose of Picrotoxin daily. Finally a dose of 1.5 mg./Kg. was given, which amount has been used by us as a standard lethal dose. The results are illustrated by Table II.

In addition, Picrotoxin was injected intramuscularly in one rabbit beginning with a dose of 1.0 mg./Kg. which was slowly increased up to 1.6 mg./Kg. After eleven such injections this animal survived 1.5 mg./Kg. intravenously. The injections were then continued and the rabbit tolerated later 1.6 and 1.7 mg./Kg. The twenty-fifth injection of 1.8 mg./Kg. proved fatal. Two other rabbits similarly treated died following the second injection of 1.5 or 1.6 mg./Kg. This demonstrates that there is only a small chance to produce tolerance and its degree remains slight. It seems, therefore, permissible to use rabbits repeatedly for Picrotoxin experiments within limits. A rest period of one week should be granted, as a rule.

III—TESTING FOR ANALEPTIC EFFICIENCY.

The testing for analeptic efficiency was performed by observing the abbreviation of a standard Nembutal sleep through increasing doses of Picrotoxin. All rabbits received 35 mg./Kg. Nembutal intravenously. The injection of Picrotoxin followed ten minutes later. We used also on this test 1.5 mg./Kg. as a unit dose for Picrotoxin. The animals were then observed and from time to time a stimulus was applied by pinching of the ears or tail. If the rabbits were able, following such a stimulus, to raise their heads and to keep them from falling to the side the animal was considered awake. This is, of course, a deliberate definition but proved to be a satisfactory criterion, after the investigator had gathered some experience with this method. The time which elapsed from the injection of the Nembutal until the awakening was called total sleeping time. Figure 1 on page 287 illustrates the relation between Picrotoxin dose and sleeping time. While the duration of sleep following an intravenous injection of 35 mg./Kg. Nembutal varies between 70 and 110 minutes, the injection of Picrotoxin abbreviates not only this period but also tends to equalize the sleeping time of different animals injected with the same dose of Picrotoxin. For the sake of brevity we refrain from giving the individual results in each series and reproduce in Table III only those with the dose of 2.25 mg./Kg. of Picrotoxin as an example.

TABLE III.—INDIVIDUAL SLEEPING TIME OF RABBITS INJECTED WITH 35 MG./KG. NEMBUTAL I. V. AND 2.25 MG./KG. PICROTOXIN I. V. 10 MINUTES LATER.

Sleeping Time in Minutes.	
52	41
44	40
40	39
41	34
53	46
44	55

Average of above 12 experiments 44.3 minutes.

TABLE IV.—ASSAY OF UNKNOWN PICROTOXIN SOLUTIONS.

Dose Given, Mg./Kg.	Dose Found, Mg./Kg.
1.5	2.25
1.5	2.30
1.5	1.80
2.0	2.45
2.5	2.50
3.5	2.50

The graph shows the number of experiments in each series. In addition the standard error of the average is given and also the standard error of the single determination which indicates how much the single results deviate from the average. These criteria indicate a satisfactory accuracy of the results. As can easily be seen from the shape of the curve the greatest steepness lies between 1.5 and 3.0 mg. Picrotoxin. The sleeping time between these two doses falls from approximately 60 to 24 minutes. We have therefore tried to use this part of the curve for an assaying of the Picrotoxin content of unknown solutions. Five rabbits were injected with Nembutal as described above and then with an amount of Picrotoxin unknown to the observer but being in the range of 1.5 to 3.0 mg./Kg. The results were plotted against the curve and compared with the dose injected. Table IV shows such experiments.

The results indicated that in this way a good indication can be obtained and furthermore that mostly the error tends to be in the direction of finding a too great dose as compared with the given one. We feel that this test is a useful supplement to the toxicity test in spite of the fact that the latter is probably more accurate in detecting small differences in dosage. With increasing doses the relative abbre-

viation of the sleeping time becomes less which makes this part of the curve less useful for assaying. With the extremely high dose of 15 mg./Kg. we found the total sleeping time cut down to fourteen minutes which means that the animal was awake four minutes after the injection of Picrotoxin.

Animals which received as much as 10.5 mg./Kg. Picrotoxin after Nembutal died later from convulsions, while 7.5 mg./Kg. were tolerated in the majority of cases. This means that the lethal dose for Picrotoxin under the influence of Nembutal as used in our experiments increases five times as compared with the unnarcotized animal. This fact illustrates the considerable therapeutic range if used as an analeptic in barbiturate poisoning.

IV—STABILITY OF PICROTOXIN SOLUTION.

Using these two methods we determined whether or not a Picrotoxin solution deteriorates while standing over a long period of time. For this purpose a solution was used which was prepared in January 1935, containing 0.3 mg. per cc. and 0.5% chlorbutanol as a preservative. It was kept at room temperature in a glass bottle with cork stopper. The reassay was done in December 1937, at which time the solution appeared completely clear and colorless. The test for toxicity and efficiency showed no deviation from the standard. Similar results were obtained with other samples tested for stability. We conclude, therefore, that no significant deterioration occurs in such solutions under ordinary circumstances within two years.

We have furthermore started a study concerning the cumulative action of Picrotoxin results of which we plan to report later. We wish, therefore, only to mention that if the dose of 1.5 mg./Kg. is given in two parts of 0.75 mg./Kg. each, convulsions and death follow in somewhat more than half of the cases, while the animals survived if the interval between the injection was one hour.

V—PICROTOXININ.

It is known that Picrotoxin can be split into two compounds, Picrotoxinin and Picrotin. The former represents the active part. Picrotoxinin is even less soluble in water, but a 0.1% solution is stable. We found its lethal dose to be 1.0 mg./Kg. intravenously. We have run a number of experiments with Picrotoxinin, counteracting Nembutal sleep with the same technique as described for Picrotoxin. The influence upon the sleeping time is principally the same as Picrotoxin. Death followed a dose of 5.0 mg./Kg. Picrotoxinin if given in Nembutal sleep. So far Picrotoxinin did not seem to offer advantages as compared with Picrotoxin.

SUMMARY.

1. Determination of the intravenous toxicity of Picrotoxin was performed on a large number of rabbits at different periods of time. The M. L. D. for fifty per cent lies between 1.2 and 1.3 mg./Kg. Approximately eighty-five per cent of the animals were killed by 1.5 mg./Kg.

2. A curve is presented showing the abbreviation of a standard Nembutal sleep by increasing doses of Picrotoxin.

3. This curve and determination of toxicity represents a satisfactory method for assaying Picrotoxin solutions.

4. No tolerance or only a slight degree, followed the repeated administration of Picrotoxin.

5. No deterioration in Picrotoxin solutions was noted within two years.

6. Some data regarding Picrotoxinin are presented.

REFERENCES.

(1) Maloney, A. H., Fitch, R. H., and Tatum, A. L., *J. Pharmacol.*, 41, 465 (1931).

(2) Maloney, A. H., Fitch, R. H., and Tatum, A. L., *Ibid.*, 44, 337 (1932).

(3) Bleckwenn, W. J., Masten, Mable G., and Tatum, A. L., *Ibid.*, 60, 99 (1937).

(4) Linegar, Charles R., Dille, James M., and Koppanyi, Theredore, *Science*, 82, 376 (1935).

(5) Linegar, Charles R., Dille, James M., and Koppanyi, Theodore, *Proc. Soc. Exptl. Biol. Med.*, 33, 396 (1935–1936).

(6) Murphy, W. S., Connerty, H. V., Connolly, A. J., and Koppanyi, Th., *J. Lab. Clin. Med.*, 22, 350 (1937).

(7) Kline, Edward M., Bigg, Edward, and Whitney, H. A. K., *J. A. M. A.*, 109, 328 (1937).

(8) Cohen, Seymour J., and Kohn, Richard, *J. Pharmacol.*, 60, 102 (1937).

(9) Heffter, A., "Handbuch der exp. Pharmakologie," Vol. 2, Part 1 (1920).

DRUG EXTRACTION. XVIII. MODIFIED DIACOLATION.*[1]

BY WILLIAM J. HUSA[2] AND C. L. HUYCK.

Experiments have been carried out to determine the efficiency of a modified diacolation process in the preparation of fluidextract of belladonna root.

HISTORICAL REVIEW.

In 1935 and 1936, H. Breddin (1), (2) was granted patents in several countries on an "Apparatus for Extracting Drugs and the Like," commonly called the diacolation apparatus. In this apparatus, the menstruum is forced from a storage bottle, by means of air pressure obtained by pressing on a rubber bulb by hand, through a throttle device and drip chamber arranged for the purpose of controlling the rate of flow of menstruum into the drug. The menstruum is slowly forced through one or more cylindrical glass tubes packed with the drug, the tubes being connected by glass tubing running from the top of one tube to the bottom of the other so that the menstruum flows upward through the drug. The object of the invention is to produce highly concentrated percolates without use of heat, and using only relatively small quantities of extraction fluid (1).

In the preparation of fluidextract of cinchona by diacolation, Breddin (3) used a battery of nine tubes, each tube being 80 cm. long and 1.7 to 1.8 cm. wide. Six hundred grams of cinchona were moistened, macerated and packed in the tubes. By means of the visible drip chamber, the menstruum was allowed to enter the drug at the rate of one and one-half drops per minute and was forced through the drug by air pressure not exceeding one and one-half atmospheres. The receiver was evacuated to facilitate penetration of the drug by the menstruum and to aid in establishing the correct rate of flow. The preparation of 600 Gm. of fluidextract from 600 Gm. of drug was completed in about twenty days.

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* Scientific Section, A. PH. A., New York meeting, 1937.

[1] This paper is based on part of a dissertation presented to the Graduate Council of the University of Florida by C. L. Huyck, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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Advantages of Diacolation.—The advantages of diacolation were stated by Breddin (4) as follows: (*a*) some drugs, notably cinchona, were not completely extracted by repetition diacolation, but were successfully exhausted by diacolation, (*b*) diacolation provided for regulation of the rate of penetration and for adjustment of length of drug column and rate of flow of percolate, (*c*) diacolation provided a quick, efficient and convenient method of preparing tinctures.

F. Gstirner (5) stated that the advantages of diacolation over maceration in the manufacture of tinctures were that less time was required, more total extractive was obtained and less menstruum was used. Tinctures were prepared by six different processes by S. von Bari (6), who concluded that diacolation gave the most promising results. K. Höll (7) found that tinctures of nux vomica, strophanthus, cinchona and ipecac made by diacolation contained a higher percentage of alkaloids than the corresponding tinctures prepared by maceration.

Disadvantages of Diacolation.—Considering diacolation from both the theoretical and practical standpoints, R. Kummer (8) outlined the following disadvantages: (*a*) from a mathematical point of view too much emphasis was placed on the form of the percolator used in the process, (*b*) from a survey of the literature the value of pressure was questionable, (*c*) the charging and discharging of the tubes was inconvenient, (*d*) too much emphasis was placed on uniform packing of the drug.

According to E. Kessler (9), diacolation was not applicable to fine powders, and the use of pressure diminished the efficiency of extraction by causing formation of passages through the drug. C. Koch (10) was of the opinion that the trouble involved in assembling a large diacolation battery for the manufacture of fluidextracts would hinder the adoption of the process. In the manufacture of tinctures of cinchona and valerian by diacolation, K. Höll (7) found that finely powdered drugs could not be used and that the powdered drugs should be mixed with ten per cent of sand before packing. Working on cinchona, Büchi and Feinstein (11) found that finely powdered drug could not be used in the preparation of the fluidextract; they concluded that the apparatus was too complex.

Drugs upon Which Diacolation Was Tested and Results Obtained.—Breddin (3) reported that he successfully prepared fluidextract of cinchona by diacolation; he also described methods of making fluidextracts of ergot, condurango, orange, frangula, hydrastis, thyme, senega, ipecac and valerian by diacolation (12). Szentgale (13) found that diacolation with a weaker alcoholic menstruum produced a better fluidextract of hydrastis than percolation, but percolation with a menstruum of the same alcoholic strength was better than diacolation in the manufacture of fluidextracts of belladonna leaves, hyoscyamus and ipecac, the conclusions being based on the content of alkaloids and total extractive matter. In preparing fluidextract of cinchona, Büchi and Feinstein (11) obtained no better results by diacolation than by ordinary percolation but declined to draw any conclusions as to the efficiency of the process until after making further tests.

EXPERIMENTAL PART.

From an examination of the patent and journal literature on diacolation it appeared that any favorable results obtained with the apparatus were due primarily to the length of the drug column. The complicated arrangements for regulating the flow of menstruum into the percolator tubes seemed unnecessary. It could hardly be expected that upward flow of the percolate against the force of gravity would add anything to the efficiency of extraction. The use of water to dis-

place the alcoholic menstruum from the exhausted drug could only replace other methods of alcohol recovery and would in no way affect the rate of extraction.

In the present study, therefore, an apparatus was constructed with the object of determining the efficiency of extraction under conditions of forced flow of menstruum through a long column of drug. As shown in the photograph, a long drug column was obtained by using flanged pipe made of Pyrex glass. Eight sections of glass pipe were joined together by means of U-shaped fittings made of Pyrex glass pipe. Interface joint gaskets made of sulfur-free gum rubber were used at the joints, which were held together by metal joint flanges. The menstruum was forced through the drug by use of compressed air. The dimensions of the tubes were as follows: Length, 91 cm.; internal diameter, 2.5 cm.; thickness of wall, 5 mm.

The apparatus had a capacity of 2400 Gm. of drug, the drug used being moderately coarsely powdered belladonna root from a 100-lb. shipment previously described (14). To determine the

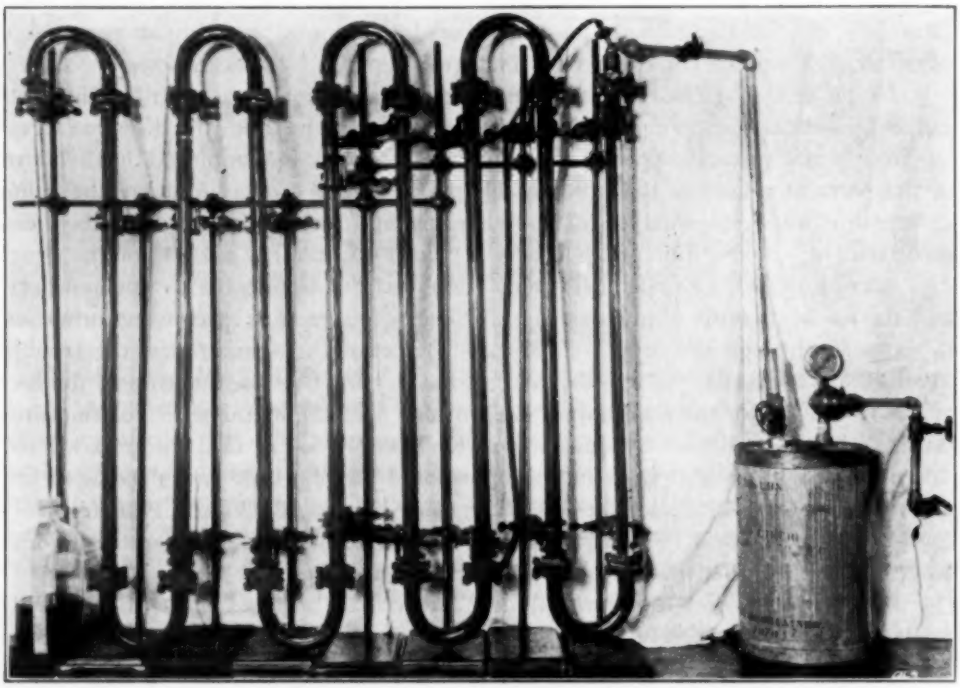

Fig. 1.—Extraction apparatus used in present study.

efficiency of the apparatus, 2400 cc. of fluidextract of belladonna root were prepared from 2400 Gm. of drug, using a menstruum of four volumes of alcohol and one volume of distilled water. In order to determine the rate of extraction at different stages the fluidextract was collected in two portions of 1200 cc. each and in addition a 1200-cc. portion of weak percolate was collected. After the experiment had been carried through once a duplicate experiment was carried out to verify the results obtained.

In describing the procedure, any differences in the rates of flow, etc., in Exps. I and II will be pointed out. In both experiments the total length of the drug column was 936 cm. and the volume of packed drug was 5120 cc. The time required for packing the drug in the tubes was about seven hours. In each case the drug was moistened with 25 cc. of menstruum per 100 Gm. of drug before packing. After packing the system was allowed to stand for 39½ hours in Exp. I and 18 hours in Exp. II. In each case the menstruum was run in at a pressure of 25 to 35 pounds per square inch. In Exp. I the menstruum had penetrated the drug in six of the tubes in 107 hours and at this point it was necessary to shut off the pressure for 48 hours, after which the pressure was again applied and after 47 additional hours the liquid had progressed through all the tubes

and had begun to drop into the receiver. In Exp. II there was no interruption and the liquid reached the end of the last tube in 164 hours or about 7 days. Data as to the time required are given in Table I and analytical data on the fluidextracts appear in Table II.

TABLE I.—PREPARATION OF FLUIDEXTRACTS OF BELLADONNA ROOT BY FORCED PERCOLATION THROUGH A LONG COLUMN OF DRUG.

	Time of Operator Required in Hours.	Total Elapsed Time in Hours.	Time Required for Collection of Percolates in Hours. First Reserve.	Second Reserve.	Weak Percolate.
Exp. I	10	317½	74½	80½	48½
Exp. II	10	405	72	101	43

TABLE II.—ANALYTICAL DATA ON FLUIDEXTRACTS OF BELLADONNA ROOT.

	Gm. Alkaloids in Percolates. Exp. I.	Exp. II.	Gm. Total Extractive in Percolates. Exp. I.	Exp. II.
First reserve 1200 cc.	13.8	14.1	168.8	173.8
Second reserve 1200 cc.	0.8	0.7	167.4	173.1
Weak percolate 1200 cc.	0.4	0.5	92.6	92.6
Total 3600 cc.	15.0	15.3	428.8	439.5
Total of first and second reserves calculated on 1000 cc.	6.1	6.2	140.1	144.5

DISCUSSION OF RESULTS.

The data in Table II show that a very high proportion of the total alkaloids is contained in the first reserve, with a much lower concentration in the second reserve and still less in the weak percolate. By collecting 2400 cc. of fluidextract from 2400 Gm. of drug, a product containing 6.1 to 6.2 Gm. of alkaloids per L. was obtained. These results show that it is possible to prepare a full strength fluidextract without concentration of weak percolates as in ordinary percolation and without collecting numerous fractions of percolates as in fractional percolation.

In comparing the alkaloidal content of the fluidextracts with that of fluidextracts made from the same shipment of drug in earlier studies (14), (15) it is seen that the apparatus and method described in the present paper gave results as good as those obtained by modified repetition diacolation and better than those obtained by the U. S. P. Processes A and C for fluidextracts. The content of alkaloids in Gm. per L. in the fluidextracts prepared in the present study was 6.1 to 6.2 as compared with an average of about 6.2 by modified repetition diacolation and about 5.8 by Processes A and C of the U. S. P. XI and N. F. VI.

In a previous study by the present authors (16) comparisons were made of the efficiencies of funnels, Oldberg percolators and cylindrical tubes; the different lengths of drug column obtained with these different percolators did not affect the final results of extraction to any great extent in ordinary percolation. However, the present study shows that when the drug column is greatly increased in length there is a marked increase in efficiency of extraction of alkaloids.

The pressure used in our experiments was obtained from the service compressed air line, the high pressure in the line being reduced to the desired figure by a reducing valve and gage. The success of this arrangement verified our previous opinion that the complicated arrangement of throttle device, drip valve, etc., as used by Breddin is superfluous; possibly some of Breddin's devices are necessary when the pressure is supplied by a rubber hand bulb but all this inconvenience is eliminated in our apparatus.

Instead of packing the drug in separate tubes and connecting these by glass tubing as was done by Breddin, our tubes were connected to each other by glass U-tubes of the same diameter. The U-tubes were packed with drug, thus forming one long continuous drug column. In this respect our apparatus differs from that of Breddin and other previous workers.

In Breddin's apparatus the flow of menstruum was upward in each tube packed with drug, and downward in the connecting glass tubes which contained none of the drug. There appears to be no special merit in this arrangement, since good results were obtained in our apparatus in which the flow was downward in four of the tubes and upward in the other four. As outlined in a previous paper (15) the use of water to displace an alcoholic menstruum from the marc is not applicable to drugs which swell and clog the percolator when water is added.

Many features of Breddin's diacolation apparatus have been known and used for many years. The method of passing the menstruum through a series of containers without collecting reserve percolates is very old, this procedure having been employed by Boullay (17) in 1833. Lalieu (18) in 1862 used a series of tubes arranged on an incline so that the liquid would flow continuously from one to the other. A series of extraction tubes connected by smaller glass tubing was employed by Catford (19) in 1898. Pressure has been used in percolation in a number of ways for more than one hundred years. Displacement of an alcoholic menstruum by water was employed many years ago by Squibb (20). Considering all these things it is difficult to see anything original or patentable in Breddin's claims (1) with the exception of the complicated arrangements for a visual drip chamber, etc., for regulating the inflow of the menstruum and our results show that this feature is by no means necessary for successful extraction.

While the use of a series of tubes is not new, our results show that the use of a long drug column leads to very efficient extraction, since a fluidextract considerably above U. S. P. strength was prepared by straight percolation without concentration of weak percolate. Naturally a long column of drug offers such resistance to flow of the liquid that pressure is necessary to force the percolation.

The forced flow of menstruum through a series of tubes may be considered as a fractional percolation process in which the menstruum flows from one percolator to the other without separating the percolate into fractions or collecting reserve percolate from the individual tubes. In using a battery of tubes, more time is required for packing and assembling and the total elapsed time is greater than in ordinary percolation or fractional percolation.

SUMMARY.

Full strength fluidextracts of belladonna root were made by slow percolation under pressure through an extremely long column of drug without resorting to collection of various fractions of weak percolate as in fractional percolation and without use of heat to concentrate weak percolate as in Process A of the U. S. P.

The apparatus devised and assembled in the present study consisted of a series of tubes of Pyrex glass pipe, connected by glass U-tubes of the same diameter. The drug was packed in one long continuous column and the menstruum forced through by compressed air.

A discussion is given of the patented extraction apparatus which is used in the process of diacolation as carried out by Breddin.

REFERENCES.

(1) Breddin, H., U. S. patent 2,046, 055; application filed April 4, 1934; patent granted June 30, 1936.

(2) Breddin, H., German patent 608,377, French patent 776,323, British patent 421,944; through *Chem. Abstr.*, 29, 2664, 3467, 4216 (1935).

(3) Breddin, H., *Pharm. Ztg.*, 79, 163 (1934).

(4) Breddin, H., *Ibid.*, 79, 148 (1934).

(5) Gstirner, F., *Apoth. Ztg.* (*Die Deutsche Apotheke*), 2, 742 (1934).

(6) von Bari, S., *Pharm. Ztg.*, 80, 852 (1935).

(7) Höll, K., *Ibid.*, 80, 1185 (1935).

(8) Kummer, R., *Ibid.*, 79, 664 (1934).

(9) Kessler, E., *Ibid.*, 79, 823 (1934).

(10) Koch, C., *Apoth. Ztg.* (*Die Deutsche Apotheke*), 2, 773 (1934).

(11) Büchi, J., and Feinstein, K., *Pharm. Acta Helv.*, 11, 341 (1936).

(12) Breddin, H., "Das Diakolationsverfahren zur eindampfunglosen Extraktion" (1934), Kirchain, N-L., pages 39–44.

(13) Szentgale, I., *Magyar Gyógyszerésztud. Társaság Értesitõje*, 12, 120 (1936); through *Chem. Abstr.*, 30, 3942 (1936).

(14) Husa, W. J., and Huyck, C. L., Jour. A. Ph. A., 27 (1938), 105.

(15) Husa, W. J., and Huyck, C. L., *Ibid.*, 27 (1938), 205.

(16) Husa, W. J., and Huyck, C. L., *Ibid.*, 27 (1938), 211.

(17) Boullay, M., *J. pharm. chim.* [2], 19, 402 (1833).

(18) Lalieu, M. A., *J. pharm. Anvers*, 18,104 (1862).

(19) Catford, J. V., *Chemist and Druggist*, 52, 271 (1898); through Proc. A. Ph. A., 47, 386 (1899).

(20) Squibb, E. R., Proc. A. Ph. A., 14, 81 (1866).

ALCOHOL CONTENT OF EXTRACTIVE PREPARATIONS.*

BY E. G. KING, LOUIS GOLDBERG, E. C. BEELER, R. K. SNYDER AND E. N. GATHERCOAL.

INTRODUCTORY.

It is required by law that the content of alcohol be stated on the label of each package of every item containing alcohol and offered for sale in interstate commerce. Manufacturers and distributors generally state this alcohol content as a single figure.

In the National Formulary the alcohol content of each preparation containing one per cent or more of alcohol is given in the monograph of such preparation with a minimum and a maximum limit. Alcohol content means the volume of C_2H_5OH present in one hundred volumes of the liquid preparation.

The official method for the determination of absolute alcohol, first introduced into U. S. P. IX, has been subject in recent years to considerable criticism, as is noted in the following papers: "Determination of Alcohol in Pharmaceutical Liquids I, Study of the U. S. P. X and U. S. P. XI Method," Jour. A. Ph. A., 25, 313–316 (1936); "Determination of Alcohol in Pharmaceutical Liquids II, a New Method," Jour. A. Ph. A., 25, 982–985 (1936). Both papers are by Karl Bambach and T. H. Rider.

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* National Formulary Research Project F 22 at the N. F. Laboratory, Chicago.

The alcohol content statements, especially of the extractive preparations in National Formularly VI, have been subject to considerable criticism during 1936. Data gathered from several manufacturers indicate that there may be a wide variation, sometimes as much as 15 percentage points in the alcohol content of the same preparation made by different manufacturers or even by the same manufacturer.

The conditions mentioned above led to the investigation reported in this paper. An endeavor is made to establish the reasons for the marked decrease in content of C_2H_5OH in the extractive preparation as compared with the C_2H_5OH content of the menstruum with which the preparation is made. It would be desirable to place C_2H_5OH content standards on a scientific basis and remove them from a purely empirical basis.

SHRINKAGE OF AQUEOUS-ALCOHOLIC MIXTURES.

While publications have appeared on this subject,[1] it was thought desirable to repeat the work for the purpose of confirming previous results.

For the preparation of the solution of the alcohol in water, the procedure was as follows:

(1) The content of C_2H_5OH in U. S. P. alcohol was determined by specific gravity. This was approximately 95.03 per cent by volume in all of the alcohol used.

(2) Cassia flasks were accurately calibrated to determine their exact volume at the lowest mark in the graduation on the neck of the flask.

(3) The calculated volume of alcohol was transferred into a tared cassia flask, and the weight of the alcohol was determined as a check on the measured volume.

(4) The calculated volume of water (recently boiled distilled water) was transferred into the same cassia flask and the weight of water was determined, as a check on the measured volume. The volume figures used in the table are those obtained from the weights of the alcohol and water taken.

(5) The volume of the liquid in the flask was accurately read in the graduation in the neck of the flask and compared to the total measured volume of the liquids added to the flask.

(6) All the work was done at 25° C.

The results appear on page 298.

NOTES.

(1) The U. S. P. XI states that Diluted Alcohol may be prepared by mixing 500 cc. of alcohol with 500 cc. of distilled water, that such a mixture measures about 970 cc. and that it contains not less than 48.4 per cent and not more than 49.5 per cent by volume at 15.56° C. of C_2H_5OH. Our mixture of 66.22 cc. of alcohol and 66.27 cc. of water showed a volume equal to 968.5 cc. on the basis of the U. S. P. statement and 48.96 per cent of C_2H_5OH, calculated on the actual volume of the diluted alcohol.

(2) The shrinkage in volume is most marked in the "50 and 60 per cent" alcohols (av. 3.15 cc.), next in the "40 per cent" alcohol (av. 3.0 cc.), next in the "80 per cent" alcohol (av. 2.18 cc.), and least in the "20 per cent" alcohol (av. 1.58 cc.).

(3) The largest increase in C_2H_5OH content is noted in the "60 per cent" alcohol (1.80 per cent); "80 per cent" alcohol comes next with 1.75 per cent; "50 per cent" alcohol third with 1.45 per cent; "40 per cent" alcohol with 1.14 per cent and "20 per cent" alcohol with 0.30 per cent increase.

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[1] Wood, H. C., Jour. A. Ph. A., 8, 730 (1919).

EXPERIMENTAL ERROR BY THE OFFICIAL METHOD FOR ALCOHOL CONTENT DETERMINATIONS.

Three similar aqueous-alcoholic mixtures were prepared and several C_2H_5OH determinations of each one were made by the U. S. P. XI method for the purpose of determining the extent of experimental error. The results were as follows:

Theoretical C_2H_5OH Content by Volume.	Experimental C_2H_5OH Content by Volume.
78.10 per cent	77.76 per cent
	77.54 per cent
	77.88 per cent
	77.40 per cent
59.32 per cent	59.07 per cent
	58.90 per cent
	59.07 per cent
	58.74 per cent
40.70 per cent	40.00 per cent
	40.20 per cent

NOTES.

(1) Glass-stoppered volumetric flasks calibrated at 25° C. were used for making these solutions. The solute was accurately weighed in the dry and tared flask. Solvent at 25° C. was added from a burette to about three-quarters of the capacity and agitated with a swirling motion. If all the solute did not dissolve in this quantity, more solvent was added to a point convenient for agitation without wetting the neck above the capacity mark. In some cases it required a day or two of standing with intermittent agitation before the material was completely dissolved and in extreme cases slight heating was necessary. After complete solution, more solvent at 25° C. was added from a burette until the meniscus was within about 0.5 cc. of the capacity mark and left to stand over night or until apparent shrinkage had ceased. The solution was then placed in a water-bath at 25° C. for fifteen minutes after which solvent was immediately added to bring the meniscus to the capacity mark. The flask and contents were then weighed.

Solvent Added by Weight.—The difference between weight of solution and solute represented the weight of solvent added. Solvent containing no solute was made up along with the individual series of solutions by the same method used in making the solutions. From this the density, Gm. per cc., at 25° C., of the solvent was determined. Knowing density and weight of solvent added, the volume of solvent was calculated as a double-check on solvent added; namely, by weight and by volume (burette).

A typical example is tannin, containing 6 per cent of moisture as determined by the U. S. P. XI toluene method, dissolved in diluted alcohol:

Weight of flask + tannin + moisture	81.6 Gm.
Weight of flask, 100 cc. capacity	49.8 Gm.
Weight of tannin + moisture	31.8 Gm.
Weight of tannin (31.8 × 0.94)	30.0 Gm.
Weight of moisture (31.8 − 30)	1.8 Gm.
Weight of flask + solution	155.8 Gm.
Weight of tannin + moisture + flask	81.6 Gm.
Weight of menstruum	74.2 Gm.

100 cc. of solvent weighed 92.6 Gm. at 25° C.

Density of solvent (92.6 ÷ 100) = 0.926 Gm. per cc.

Volume of solvent added by weight (74.2 ÷ 0.926) = 80.1 cc.

Volume of solvent added by volume (burette) = 79.9 cc.

Volume displaced by 30 Gm. of tannin:

(*a*) By volume (burette) 100 − (79.9 + 1.8) = 18.3 cc.
(1.8 is the volume of moisture in the tannin as used)

(*b*) By weight 100 − (80.1 + 1.8) = 18.1 cc.

Sample No.	Volume in Cc's. of				Shrinkage in Volume.		Percentage of U. S. P. Alcohol.			Percentage of C_2H_5OH at 15.56° C.		
	Alcohol Used.	Water Used.	Total Used.	Actual in Flask.	In Cc.	In %.	In the Theoret. Volume.	In the Actual Volume.	Increase.	In the Theoret. Volume.	In the Actual Volume.	Increase.
	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.
1(*a*)	108.18	27.03	135.21	132.25	2.96	2.24	80.00	81.80	1.80	76.02	77.73	1.71
1(*b*)	105.68	26.56	132.24	129.49	2.75	2.12	79.92	81.80	1.88	75.94	77.73	1.79
2(*a*)	79.32	52.65	131.97	128.00	3.97	3.10	60.10	61.97	1.87	57.11	58.88	1.77
2(*b*)	79.12	53.09	132.21	128.10	4.11	3.21	59.85	61.76	1.91	56.87	58.69	1.82
3(*a*)	65.93	66.39	132.32	128.24	4.08	3.18	49.83	51.41	1.58	47.42	48.85	1.43
3(*b*)	66.22	66.27	132.49	128.44	4.05	3.15	49.97	51.52	1.55	47.48	48.96	1.48
4(*a*)	54.14	78.89	134.03	130.25	3.78	2.89	40.38	41.57	1.19	38.37	39.50	1.13
4(*b*)	54.23	81.36	135.59	131.60	3.99	3.03	40.00	41.21	1.21	38.01	39.16	1.15
5(*a*)	26.17	104.88	131.05	129.00	2.05	1.60	19.97	20.29	0.32	18.98	19.28	0.30
5(*b*)	26.31	105.43	131.74	129.70	2.04	1.57	19.97	20.29	0.32	18.98	19.28	0.30

1st column: Volume of U. S. P. alcohol used.
2nd column: Volume of distilled water used.
3rd column: Total volume of liquids added to the flask.
4th column: Actual volume of liquid as measured in the flask.
5th column: Shrinkage in volume in cc.
6th column: Shrinkage in volume in per cent, based on the actual volume in the flask.
7th column: Calculated percentage of U. S. P. alcohol by volume in the theoretical volume of the mixed liquids.
8th column: Calculated percentage of U. S. P. alcohol by volume in the actual volume of the mixed liquids.
9th column: Increase in percentage of U. S. P. alcohol in the actual volume as compared with that in the theoretical volume.
10th column: Calculated percentage of C_2H_5OH by volume in the theoretical volume of the mixed liquids.
11th column: Calculated percentage of C_2H_5OH by volume in the actual volume of the mixed liquids.
12th column: Increase in percentage of C_2H_5OH in the actual volume as compared with that in the theoretical volume.

EFFECT OF SOLUTES ON VOLUME INCREASE AND ALCOHOL-CONTENT DECREASE* (1).

	Solute Used.	Solvent Added.	Displacement by Solute.	C_2H_5OH Decrease (5). Calculated.	C_2H_5OH Decrease (5). Determined.
Solute: Dextrose (6)	5 Gm.	96.9 cc.	3.1 cc.	....	....
Solvent: Water (2)	10 Gm.	93.7 cc.	6.3 cc.	....	....
	15 Gm.	90.6 cc.	9.4 cc.	....	....
	20 Gm.	87.6 cc.	12.4 cc.	....	....
	25 Gm.	84.3 cc.	15.7 cc.	....	....
	50 Gm.	69.1 cc.	30.9 cc.	....	....
	5 Gm. Av.	96.9 cc.	3.1 cc.	....	....
Solute: Dextrose	5 Gm.	96.7 cc.	3.3 cc.	1.6%	....
Solvent:	10 Gm.	93.5 cc.	6.5 cc.	3.1%	....
Alcohol, 1 vol.,	15 Gm.	90.4 cc.	9.6 cc.	4.6%	....
Water, 1 vol. (4)	20 Gm.	87.2 cc.	12.8 cc.	6.2%	....
	25 Gm.	83.6 cc.	16.4 cc.	8.0%	....
	5 Gm. Av.	96.8 cc.	3.2 cc.	1.6%	....
Solute: Tannin (3)	10 Gm.	94.4 cc.	5.6 cc.	....	....
Solvent: Water (2)	20 Gm.	88.7 cc.	11.3 cc.	....	....
	30 Gm.	82.1 cc.	17.9 cc.	....	....
	40 Gm.	76.2 cc.	23.8 cc.	....	....
	50 Gm.	70.9 cc.	29.1 cc.	....	....
	5 Gm. Av.	97.1 cc.	2.9 cc.	....	....
Solute: Tannin	10 Gm.	93.9 cc.	6.1 cc.	3.2%	2.8%
Solvent:	20 Gm.	87.8 cc.	12.2 cc.	6.4%	6.3%
Alcohol, 1 vol.,	30 Gm.	81.7 cc.	18.3 cc.	9.7%	9.7%
Water, 1 vol. (4)	40 Gm.	75.7 cc.	24.3 cc.	12.8%	12.8%
	50 Gm.	69.5 cc.	30.5 cc.	16.1%	16.3%
	5 Gm. Av.	97.0 cc.	3.0 cc.	1.6%	1.6%
Solute: Tannin	10 Gm.	94.4 cc.	5.6 cc.	5.3%	4.4%
Solvent:	20 Gm.	88.7 cc.	11.3 cc.	10.7%	10.9%
Alcohol, 9 vol.,	30 Gm.	82.9 cc.	17.1 cc.	16.2%	16.9%
Water, 1 vol. (4)	40 Gm.	76.9 cc.	23.1 cc.	21.8%	22.4%
	50 Gm.	70.8 cc.	29.2 cc.	27.6%	28.8%
	5 Gm. Av.	97.1 cc.	2.9 cc.	2.8%	2.8%
Solute:					
Sodium Chloride (10)	20 Gm.	92.7 cc.	7.3 cc.	....	....
Solvent: Water (2)	5 Gm. Av.	98.2 cc.	1.8 cc.	....	....
Solute: Gentian Ex. (7)	20.6 Gm.	85.8 cc.	14.2 cc.	6.9%	4.9%
Solvent:	30.6 Gm.	78.6 cc.	21.4 cc.	10.4%	7.0%
Alcohol, 1 vol.,	40.2 Gm.	72.0 cc.	28.0 cc.	13.5%	9.1%
Water, 1 vol.	5.0 Gm. Av.	96.5 cc.	3.5 cc.	1.7%	1.2%
Solute:	5.3 Gm.	95.8 cc.	4.2 cc.	3.6%	2.9%
Resin of Ipomea (8)	5.7 Gm.	95.6 cc.	4.4 cc.	3.7%	3.1%
Solvent:	10.2 Gm.	92.6 cc.	7.4 cc.	6.3%	7.0%
Alcohol, 9 vol.,	14.1 Gm.	87.8 cc.	12.2 cc.	10.4%	10.0%
Water, 1 vol. (4)	14.9 Gm.	87.2 cc.	12.8 cc.	10.9%	9.8%
	20.1 Gm.	83.6 cc.	16.4 cc.	13.9%	13.6%
	21.6 Gm.	81.8 cc.	18.2 cc.	15.5%	14.7%
	5.0 Gm. Av.	95.9 cc.	4.1 cc.	3.5%	3.3%

* The reference numbers refer to "Notes" that follow the tabulation.

Displacement by solute in the foregoing table is based on solvent added by volume as in (*a*).

(2) Distilled water was boiled fifteen minutes and used immediately after cooling. The procedure for making these solutions was the same as described in (1).

(3) Flake tannin of U. S. P. quality was used which contained 6 per cent of moisture, determined according to U. S. P. XI toluene method.

(4) The alcohol-water mixtures were prepared by mixing the required volumes of U. S. P. alcohol and recently distilled water in clean volumetric flasks, calibrated to deliver and to contain a definite volume at 25° C.

The U. S. P. alcohol used gave a sp. gr. value which corresponded to 95.34 per cent of C_2H_5OH.

On the basis of a 3 per cent shrinkage in the 50 per cent alcohol-water mixture (see page 4) the calculated content of C_2H_5OH is 49.1 per cent. Our determinations by the U. S. P. distillation method repeated on the same lot gave from 48.0 to 48.8 per cent or an average of 48.3 per cent.

The mixture of alcohol 9 volumes, water 1 volume shrinks *about* 2 per cent (see page 4) and contains about 87 per cent of C_2H_5OH by calculation. Our determinations gave an average content of 86.2 per cent before distillation and 85.6 per cent after distillation.

(5) The alcohol content was determined by the official U. S. P. XI distillation method. The calculated alcohol decrease is based on the volume of menstruum added, assuming no loss in transfer and that all alcohol in the transfer is in solution as C_2H_5OH. Theoretically, the decrease in alcohol is proportional to the volume of solute in the solution.

(6) Granulated dextrose of C.P. quality was used. The U. S. P. XI toluene method indicated 0.07 per cent of moisture. Weighings were made on the laboratory balance.

(7) Gentian extract, obtained by drying a sufficient quantity of fluidextract of gentian, made in this laboratory, in an evaporating dish on the water-bath at a maximum temperature of 70° C. to a gummy mass, was dehydrated in a vacuum desiccator over magnesium perchlorate. It was assumed to contain no moisture after an accurately weighed sample, powdered to 40 mesh, reached constant weight.

(8) Finely powdered resin of ipomea, prepared in this laboratory, was dried for two days in a vacuum desiccator over magnesium perchlorate. Since resin decomposes with continued heating it was undesirable to dry in the oven. A quantity of the resin was not available to determine moisture according to the toluene method, U. S. P. XI. Therefore, it was assumed to be completely dehydrated. Weighings of flask, solute and solution were made on the analytical balance.

(9) Density at 25° C. was determined by weighing a sample of the solute in a dry acid-tared pycnometer to one-third its volume capacity. The pycnometer was filled with xylene at 25° C., in which the test materials are insoluble, and weighed. From the density of xylene at 25° C., the volume of xylene necessary to fill the pycnometer was calculated from the weight of xylene added. This subtracted from the capacity of the pycnometer at 25° C. gave the volume occupied by the sample (solute). The weight of the sample (solute) divided by its volume gave the density, Gm. per cc. at 25 ° C.

The densities found are as follows:

Dextrose—1.521 at 25° C.
Tannin—1.406 at 25° C.
Gentian Extract—1.414 at 25° C.
Sodium Chloride—2.17 (from the Chemical Handbook, 1928).

(10) Powdered sodium chloride of C.P. quality dried to constant weight at 95° C. was used.

EFFECT OF MOISTURE IN THE DRUG.

These tinctures were prepared by the official method, using 200 Gm. of drug for one liter of tincture.

	C_2H_5OH Content.	Extractive (W/V).
Menstruum, 4 determinations	48.0%	
1 Gentian, commercial, No. 40 powder; moisture content, toluene method, 5.2%	46.0%	8.0 %
2 Gentian, dried at 100° C.; moisture content 0.0%	46.4%	8.3 %
3 Gentian, hydrated in desiccator 24 hours; moisture content 7.4%	46.1%	7.7 %
4 No. 1 repeated	46.0%	6.76%
5 No. 2 repeated	46.8%	7.04%
6 Gentian, 200 Gm., sprayed with 7 cc. of water and hydrated in desiccator for 12 hours; moisture content, toluene method, 9%	45.6%	6.14%
7 No. 6 ditto, except sprayed with 20 cc. of water; moisture content 13.6%	45.2%	6.12%
8 No. 6 ditto, except sprayed with 28 cc. of water; moisture content 16.25%	45.0%	5.99%
9 No. 6 ditto, except sprayed with 29 cc. of water; moisture content 17.5%	45.0%	5.84%

NOTES.

(1) The extractive present in the tinctures would increase the volume and thus decrease the alcohol content from 1.3 to 2 per cent.

(2) The effect of the water in the drug, even up to 16–17 per cent, did not reduce the alcohol content more than 1.7 per cent. If all the maximum amount of water in the drug (35 cc. in 200 Gm.) were added to 1000 cc. of the solvent, it would reduce the alcohol content of the mixture only 1.7 per cent.

The following "fluidextracts" were prepared in Oldberg glass percolators by collecting 500 cc. of "reserve" percolate from 500 Gm. of drug. The purpose is to demonstrate the effect of moisture in the "drug" on the alcohol content of the percolate. Every effort was made to prevent loss of alcohol during manipulation.

	Moisture in Drug.	Extractive. In Reserve Percolate.	Alcohol Content. In Menstruum.	Alcohol Content. In Percolate.	Alcohol Content. Total Decrease.	Alcohol Content. Decrease Due to Moisture in Drug (1).
Sawdust (2)	0.4%	0.9%	48.3%	48.3%	0.0%	0.0%
Sawdust	6.8%	2.4%	94.8%	91.2%	3.6%	2.0%
Sawdust	7.6%	0.9%	49.0%	46.7%	2.3%	2.0%
Sawdust	13.7%	1.0%	48.8%	44.4%	4.4%	4.1%
Sawdust	21.2%	0.4%	48.9%	41.7%	7.2%	7.0%
Starch (3)	12.0%	0.1%	94.8%	90.6%	3.2%	3.2%
Cotton (4)	4.0%	0.2%	94.0%	93.4%	0.6%	0.6%
Gentian (5)						
Commercial	8.0%	35.6%	48.9%	36.9%	12.0%	3.5%
Dehydrated	1.9%	35.6%	48.9%	38.7%	10.2%	1.7%

NOTES.

(1) These figures are based on the following assumptions:

"95 per cent" alcohol is decreased 3.3 per cent per 5 Gm. of solute.

"50 per cent" alcohol is decreased 1.6 per cent per 5 Gm. of solute, except by gentian extract, which reduces the alcohol 1.2 per cent per 5 Gm. of the solute.

After the decrease due to solute is deducted, the remainder is considered as due to "moisture in the drug."

(2) A commercial grade of sawdust was refluxed with U. S. P. alcohol to extract some of the soluble materials, then dried in the oven at 95° C. to constant weight, then varying amounts of moisture were incorporated; except that the sawdust for the second preparation was used as received.

(3) A 500-Gm. sample of corn starch, mixed with four times its weight of dried and purified sand to prevent packing, was prepared in an Oldberg glass percolator. A reserve of 500 cc. was collected. Care was taken to prevent loss of alcohol during the process.

(4) A 250-Gm. lot of cotton batting was used and 250 cc. of reserve were collected. The process was identical to that described above.

(5) The gentian percolates were collected in liter lots from 1000-Gm. lots of the powdered drug. Dehydrated gentian was prepared by drying powdered gentian under reduced pressure at 65° C. to constant weight.

SUMMARY.

(1) Determinations of the shrinkage of aqueous-alcoholic mixtures indicate that "50 per cent" and "60 per cent" alcohols show a decrease in volume of about 3.15 per cent over theoretical, "40 per cent" alcohol decreases about 2.95 per cent, "80 per cent" alcohol about 2.20 per cent, and "20 per cent" alcohol about 1.60 per cent. The calculated increase in percentage of C_2H_5OH, due to the shrinkage in volume, averages 1.77 per cent for the "60" and "80 per cent" alcohols, 1.45 per cent for the "50 per cent" alcohol, 1.14 per cent for the "40 per cent" alcohol and 0.30 per cent for the "20 per cent" alcohol.

(2) Actual determination of the C_2H_5OH content of aqueous-alcoholic mixtures by the official distillation method gave results always lower than the theoretical, the average of many results being 0.70 of a percentage point. With solutions of vegetable extractive matter containing no volatile matter except alcohol and water, the average of many determinations was 0.76 of a percentage point lower than the theoretical value. This loss may be due in part to loss of C_2H_5OH during manipulation.

(3) The average displacement in 100 cc. of solution produced by 5 Gm. of tannin in water is 2.9 cc., in "50 per cent" alcohol is 3.0 cc., and in "90 per cent" alcohol the displacement is 2.9 cc. The reduction in C_2H_5OH content averages 1.6 per cent in "50 per cent" alcohol for each 5 Gm. of solute and in "90 per cent" alcohol 2.8 per cent for each 5 Gm. of solute.

Dextrose in water gave an average displacement of 3.1 cc. per 5 Gm. of solute; in "50 per cent" alcohol it displaced 3.2 cc. with a decrease of 1.6 per cent in C_2H_5OH content per 5 Gm. of solute.

Gentian extract dissolved in "50 per cent" alcohol displaced 3.5 cc. and decreased the C_2H_5OH content, by actual determination, to 1.2 per cent per 5 Gm. of the solute.

Resin of Ipomea dissolved in "90 per cent" alcohol caused an average displacement of 4.1 cc. with a consequent reduction in alcohol of 3.3 per cent per 5 Gm. of solute.

Sodium chloride, which ionizes in water solution, gave an average displacement of 1.8 cc. per 5 Gm. of solute.

(4) Evidence indicates that the effect of "tissue" moisture in crude drug has only a slight influence on the alcohol content of a tincture or fluidextract. The amount of "free or absorbed" water in the crude drug proportionally decreases the alcohol content of a fluidextract. There was found to be an average of 0.4% decrease in alcohol content for each per cent of "free" moisture in the crude drug.

(5) Moisture in the pilular extract obtained from the "weak" percolate has an influence on the alcohol content of the fluidextract equivalent to the same

amount of water. A "soft" pilular extract seldom contains more than 25 per cent of water; a "thin" extract contains a variable amount of water depending upon its "thinness." This extract should be evaporated to such a volume that enough alcohol can be added to it to bring the solution of it to the same alcohol content as that of the reserve percolate and yet keep it within the permitted volume.

(6) There is good evidence to believe that a considerable proportion of the decrease in C_2H_5OH content of extractive preparations as compared with the C_2H_5OH content of the menstruum from which they were prepared is due to loss of alcohol by evaporation during the manufacturing process. By the exercise of care to prevent the loss of alcohol by evaporation, it was possible to increase the C_2H_5OH content of fluidextracts by 5 to 6 percentage points. While variations in extractive from different lots of the same drug may be responsible for some of the variations in C_2H_5OH content of the extractive preparations of that drug, yet probably a principal reason for these variations is the loss of alcohol by evaporation during the manufacturing process.

THE SYNTHESIS AND PHARMACOLOGICAL ACTION OF SOME 2,2,2-TRIALKYL ETHANOLS.*, **

BY ROBB V. RICE,[1] GLENN L. JENKINS[2] AND WILTON C. HARDEN.

In a study of some hydroxybenzyl alcohols Dunning, Dunning and Reid (1) found that 5-bromo-2-hydroxy and 5-ethyl-2-hydroxy benzyl alcohol possess a local anesthetic efficiency of the same relative order and it was thought possible that such a relationship might be found between other series of halogen and alkyl substituted derivatives of the same parent substance. In order to investigate this possibility four trialkyl ethanols, namely, 2,2,2-trimethyl ethanol; 2,2-dimethyl-2-ethyl ethanol; 2,2-diethyl-2-methyl ethanol and 2,2,2-triethyl ethanol were prepared and their anesthetic properties compared to those of 2,2,2-tribromoethanol which has found some use as a general anesthetic.

The method of preparation used in all cases was a modification of the one employed by Conant, Webb and Mendum (2) for preparing alcohols of the general type $R_3C\text{-}CH_2OH$. It involves three steps, namely, (*a*) preparation of the proper tertiary chloride from the corresponding alcohol by treatment with concentrated hydrochloric acid, (*b*) formation of the Grignard reagent of the tertiary chloride and (*c*) treatment of the Grignard reagent with gaseous formaldehyde followed by hydrolysis.

EXPERIMENTAL.

A description of the method employed for obtaining 2,2,2-trimethyl ethanol and an examination of Tables I and II adequately describes the preparation of all four of these compounds.

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* Scientific Section, A. PH. A., New York meeting, 1937.

** Abstracted in part from a thesis by Robb V. Rice, presented to the graduate faculty of the University of Maryland in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June 1937.

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Tertiary butyl chloride was obtained in 77–83 per cent yields by the method of Norris and Olmsted (3). Two hundred cubic centimeters of tertiary butyl alcohol (Eastman practical) and 500 cc. of concentrated hydrochloric acid were placed in a one-liter separatory funnel and shaken continuously for fifteen minutes. The layers were allowed to separate and the upper portion drawn off and washed with a saturated solution of sodium bicarbonate until it was no longer acid to litmus paper. The chloride was then dried over 20 Gm. of calcium chloride and distilled through a 20-cm. glass bead column over a water-bath. The fraction distilling at 51–52° C. was collected and kept over anhydrous sodium carbonate until ready for use.

The procedure of Puntambeker and Zoellner (4) was followed to obtain tertiary butyl magnesium chloride. Sixty-one grams (2.5 moles) of magnesium turnings were placed in a three-liter, three-necked flask fitted with a mechanical stirrer and mercury seal, a 300-cc. separatory funnel and reflux condenser. The magnesium was covered with 200 cc. of anhydrous ether followed by 5 cc. of ethyl bromide and a crystal of iodine to initiate the reaction. Stirring was started and a solution of 227 Gm. (2.45 moles) of tertiary butyl chloride in 1100 cc. of anhydrous ether was dropped slowly on the magnesium during a period of six hours. The rate of addition was regulated so that slow refluxing continued throughout the reaction. After complete addition of the halide solution, the mixture was stirred for fifteen minutes to complete the reaction.

The yield of Grignard reagent was calculated after titrating an aliquot portion of the ether solution according to the method of Gilman (5) and treated with a ten per cent excess of formaldehyde gas by heating the proper quantity of paraformaldehyde (dried over concentrated sulfuric acid for ten days) in a large test-tube connected to the reaction flask by a large-bore delivery tube. During the reaction stirring was continued and the rate of addition of formaldehyde so adjusted that gentle refluxing continued throughout the procedure. Refluxing was maintained for two hours after all the formaldehyde had been added by warming the flask on a water-bath.

TABLE I.—PREPARATION OF THE GRIGNARD REAGENTS.

Grignard Reagent.	Moles Mg. Used.	Cc. Ether Added to Mg.	Moles Chloride Used.	Cc. Ether Added to Chloride.	Time of Addition.	Yield.
I	2.5	200	2.45	1100	6 hrs.	85%
II	2.5	200	2.45	1100	8 hrs.	75%
III	2.5	200	2.5	1000	8 hrs.	65%
IV	2.23	500	2.20	800	8 hrs.	40%

I. Tert. butyl magnesium chloride.
II. Tert. amyl magnesium chloride.
III. Diethyl-methyl-carbinyl magnesium chloride.
IV. Triethyl-carbinyl magnesium chloride.

In preparing Compounds II, III and IV the reaction was carried out under an atmosphere of nitrogen to protect the Grignard reagent from the action of the air.

TABLE II.—PREPARATION OF THE SUBSTITUTED ETHANOLS.

Alcohol Prepared.	Chloride Used and % Yield.	Yield of Alcohol from Grig. Reag.	Overall Yield.	B. P.	n_D^{20} Degrees.
A	$(CH_3)_3C—Cl$ 80%	35%	30%	111–113 C.	Solid
B	$(CH_3)_2(C_2H_5)C—Cl$ 80%	33%	25%	134–135 C.	1.4203
C	$CH_3(C_2H_5)_2C—Cl$ 77%	40%	26%	150–151 C.	1.4261
D	$(C_2H_5)_3C—Cl$ 85%	10%	4%	76–77 C. at 11 mm.	1.4400

A. 2,2,2-trimethyl ethanol.
B. 2,2-dimethyl-2-ethyl ethanol.
C. 2,2-diethyl-2-methyl ethanol.
D. 2,2,2-triethyl ethanol.

Hydrolysis of the product was accomplished by pouring it onto a mixture of 1500 Gm. of cracked ice, 300 cc. of water and 300 Gm. of ammonium chloride with frequent stirring. After separating the ether layer, the aqueous portion was extracted with three 100-cc. portions of ether

and the combined ether solutions were distilled on a water-bath until most of the ether was removed. The residue was dried for several hours over anhydrous sodium sulfate. Subsequent fractionation yielded 88–95 Gm. of product, b. p. 111–113° C., m. p. 49° C.

PHARMACOLOGICAL RESULTS.

In comparing the four alchols prepared to the action of 2,2,2-tribromoethanol two different media were employed: (*a*) a ten per cent or a one per cent solution in olive oil and (*b*) a ten per cent or a one per cent solution in 95 per cent ethyl alcohol. Pharmacological studies were carried out upon mice, rats, guinea pigs and cats.

When 1–2-cc. doses of the one per cent alcohol solution were administered by rectum to rats and guinea pigs, 2,2,2-tribromoethanol was the only one found to produce complete narcosis. 2,2-diethyl-butanol-1 in doses of 3 cc. of the alcohol solution produced only a partial narcosis in guinea pigs while 4-cc. doses of 2,2-dimethyl-propanol-1 solution caused only a mild depression.

One per cent solutions of the compounds in olive oil were injected intraperitoneally in mice and the relative dosage required to produce narcosis or depression was determined. It was found that administration of 0.75 cc. of the one per cent solution of 2,2,2-tribromethanol to mice weighing 20 Gm. would produce complete narcosis which lasted about ten hours and sometimes resulted in death. One cubic centimeter of 2,2-diethyl-butanol-1, 1.2 cc. of 2-ethyl-2-methyl-butanol-1, 1.5 cc. of 2,2-dimethyl-butanol-1 and 2.1 cc. of 2,2-dimethyl-propanol-1 produced unconsciousness but of a shorter duration than the halogenated ethanol. A dose of about 8 cc. of 95 per cent ethyl alcohol was necessary to produce the same result.

Cats anesthetized with ether were injected through the fermoral vein with the respective solutions and the blood pressure taken from the carotid artery. A ten per cent solution of the compound to be tested in 95 per cent alcohol was injected slowly in doses of 0.5 cc. diluted to 10 cc. with normal saline solution. In this dose 2,2,2-tribromoethanol produced a partial paralysis of the respiration and depression of the circulation, followed by slow recovery. 2,2-diethyl-butanol-1; 2-ethyl-2-methyl-butanol-1 and 2,2-dimethyl-propanol-1 produced a similar result but in a progressively lesser degree. Most peculiarly 2,2-dimethyl-butanol-1 in the same dose was very toxic causing complete paralysis of the respiration and stoppage of the heart. Control solutions of 5 per cent ethyl alcohol had very little effect upon the circulation and produced only a slight depression of the respiration.

It was found that these alcohols will also produce their effects by absorption through the skin. When one cc. of a ten per cent solution of 2,2,2-tribromoethanol was placed on the intact skin of mice, it was rapidly absorbed to produce anesthesia lasting over twleve hours and followed by recovery. 2,2-diethyl-butanol-1; 2-ethyl-2-methyl-butanol-1; 2,2-dimethyl-butanol-1 and 2,2-dimethyl-propanol-1 were all absorbed but as found in other experiments, their effects became increasingly less as more methyl groups replaced the ethyl groups of the substituted ethanol. Ninety-five per cent ethyl alcohol (the dilution medium used above) produced no effect other than slight discomfort due to the cooling of the skin as the alcohol evaporated.

SUMMARY.

Four closely related 2,2-trialkyl ethanols have been prepared and a preliminary investigation of their pharmacological properties has shown that they all possess anesthetic action although to a much lesser degree than 2,2,2-tribromoethanol to which they were compared.

The authors are indebted to Dr. David I. Macht of Hynson, Westcott and Dunning, Inc., for his help in determining the pharmacological properties of these compounds.

REFERENCES.

(1) Dunning, B., Jr., Dunning, F., and Reid, E. E., *J. Am. Chem. Soc.*, 58, 1567 (1936).
(2) Conant, J. B., Webb and Mendum, *Ibid.*, 51, 1246–1254 (1929).
(3) Norris and Olmsted, "Organic Synthesis," 8, 50 (1928).
(4) Puntambeker and Zoellner, *Ibid.*, 8, 104 (1928).
(5) Gilman, H., and co-workers, *J. Am. Chem. Soc.*, 45, 150 (1923).

A RAPID METHOD FOR THE ASSAY OF SILVER PROTEINATES.*

BY MARGARET C. SWISHER.[1]

The U. S. P. assay for silver proteinates directs the carbonization of the weighed sample, the solution of the residue in nitric acid, the filtration of the diluted solution and the titration of the silver salt with standard ammonium thiocyanate. This is a time-consuming procedure, requiring the use of four containers and the transfer of the sample four times.

Other methods for the analysis of silver proteinates have been reported in which, for oxidizing agents, are used an acid solution of potassium permanganate (1), fuming sulfuric acid and thirty per cent hydrogen peroxide (2), mixtures of nitric and sulfuric acids (3) and perchloric acid (4).

Experience with the foregoing methods for analysis suggested that a simple and more rapid, but just as accurate a procedure for the assay of silver proteinates might be developed. With this purpose in mind, samples of silver proteinates were subjected (*a*) to analysis by the previously reported methods and their possible variations, (*b*) to treatment with other oxidizing agents and catalysts and (*c*) to methods requiring less cumbersome apparatus and technique until the following method was developed.

METHOD.

About 5 Gm. of the sample are weighed and transferred to a 50-cc. volumetric flask containing 25 cc. of water. When solution is complete, the volume is made to 50 cc. with water and mixed. To a 250-cc. wide-mouthed Erlenmeyer flask are added an accurately measured 10-cc. sample of the silver proteinate solution, 15 cc. of H_2SO_4 (sp. gr. 1.83), 1.5 cc. of fuming HNO_3 and some glass beads or broken glass tubing. The mixture is boiled over a free flame, with continuous shaking, until dense white fumes are evolved. After cooling for from one to three minutes (the solution is usually a dark red color), 1 cc. of fuming HNO_3 is added and the mixture boiled again to white fumes. If the hot solution is a lemon-yellow color, it will usually become colorless when cooled to room temperature, and the oxidation is complete. If the solution is not colorless when cold, 1 cc. of fuming HNO_3 is added, and the boiling to the white fume stage repeated. When the oxidation is complete, 50 cc. of water is added, and the solution is boiled to remove the oxides of nitrogen. The volume is brought to 100 cc. with water, the solution is cooled to room temperature, 3 cc. of ferric alum T.S. is added and the silver salt titrated with standard ammonium thiocyanate.

The entire oxidation period requires from five to twenty minutes, depending almost entirely upon the will of the operator. Weighed samples of the solid may be used in place of the solution, thus eliminating the time required to remove the solvent. The time can be further shortened if, after reaching the white fume stage the first time, the fuming HNO_3 is added drop by drop to the boiling solution while it is continuously shaken.

Although it was found that the addition of 0.2 Gm. of selenious acid to the oxidizing mixture increased the rate of oxidation, it was not generally used for the analyses in this report since the difference in time is small.

Inabinette (5) reports that samples of silver proteinate boiled with nitric acid, cooled and titrated with thiocyanate, gave results identical with those obtained by the U. S. P. method. This is true with some products, but with others Inabinette's method gives results three per cent lower than that of the U. S. P. Without the use of heat, results comparable to those by Inabinette's method can be obtained. The proteinates dissolve in and are decolorized by cold nitric acid. The results are, however, from five-tenths to three per cent low.

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* Scientific Section, A. PH. A., New York meeting, 1937.

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Since the method of the Association of Official Agricultural Chemists gives the same results as that of the U. S. P., and is easier to use, the analyses by the new method were checked against it. Over one hundred and fifty analyses were run by this method. Six different preparations of silver proteinates, which represent three of the four different types, were used. No work was done on the electric type of solution.

TABLE I.

Method Used, Time for Digestion.	A. O. A. C. 45–90 Min., % Ag.	New Method 5–20 Min., % Ag.
Strong Silver Protein (Merck)	8.19	8.21
Mild Silver Protein (Merck)	19.54	19.59
Argyrol	20.95	20.95
Silloid	17.67	17.67
Collargol	78.22	78.42

A ten per cent Argyrol ointment (Norwich Pharmacal Co.) was analyzed by this method. For complete oxidation it required from one to two hours and the use of 50 cc. of H_2SO_4 and 50 cc. of fuming HNO_3. The results indicated the presence of 2.15% silver, $\pm 0.02\%$. Samples of the same ointment were treated by the A. O. A. C. method. After heating for two days and repeatedly adding HNO_3 and H_2SO_4, the samples were discarded.

SUMMARY.

1. An accurate method, considerably less involved than that of the U. S. P., has been developed for the assay of silver proteinates.

2. It has the following advantages over that of the U. S. P. and other methods reported in the literature:

(*a*) It gives the same or slightly higher percentage of silver.

(*b*) The oxidation is complete in from one-tenth to one-third of the time.

(*c*) The complete analysis is made in one container, a 250-cc. Erlenmeyer flask.

3. It can be used for the analysis of oil solutions and of ointments of silver proteinates.

REFERENCES.

(1) Marschner, J., *Apoth. Ztg.*, 27, 887 (1912).
(2) Tabern, D. L., and Shelberg, E. F., *Ind. Eng. Chem., Anal. Ed.*, 4, 401–403 (1932).
(3) Eaton, E. O., *J. Assoc. Official Agr. Chem.*, 8, 551–552 (1925).
(4) Antoine, Georges, *J. pharm. chim.*, 21, 457–465 (1935).
(5) Inabinette, I. H., *Am. J. Pharm.*, 103, 42 (1931).

COMPARATIVE SENSITIVITY OF THE TOAD AND THE FROG TO CYMARIN AND COUMINGINE.*

BY K. K. CHEN, CHSETER C. HARGREAVES AND WILLIAM T. WINCHESTER.[1]

In a previous report (1), it was concluded that the nebulous toad, *Bufo valliceps*, was many times more tolerant to *G*-strophanthin and scillaren B than the common frog, *Rana pipiens*. It was also noted that the tolerance of the toad is confined to the cardiac muscles. Of a large number of crystalline cardiac principles studied

* Scientific Section, A. PH. A., New York meeting, 1937.

[1] From the Lilly Research Laboratories, Indianapolis, Indiana.

in this laboratory (2), (3), there were two, coumingine hydrochloride and cymarin, that were sufficiently soluble in water to be suitable for administration to toads. The purpose of this communication is therefore to present additional data demonstrating the natural tolerance of the toad to cardiac drugs, irrespective of their origin, as compared with the frog. The same species of animals were employed as before, that is, *Bufo valliceps* to represent the toad, and *Rana pipiens*, the frog. The specimen of cymarin was courteously supplied by Dr. Walter A. Jacobs, the Rockefeller Institute for Medical Research, New York City, and that of coumingine hydrochloride by Dr. Gustavo Dalma, Provincial Chemical Laboratory, Fiume, Italy. To determine the minimal systolic dose in toads, a 1 per cent solution of coumingine hydrochloride in saline, and a 2 per cent solution of cymarin with 57 per cent ethyl alcohol by volume, were prepared. For frogs, however, a 1:20,000 concentration of cymarin and 1:2000 concentration of coumingine hydrochloride, were adequate for injection purposes. The procedure of testing conforms to the U. S. P. one-hour method (4), the temperature of the bath being kept at 20° C.

TABLE I.—DETERMINATION OF MINIMAL SYSTOLIC DOSES OF OUABAIN-MERCK, COUMINGINE HYDROCHLORIDE AND CYMARIN.

Drug.	*Rana pipiens.* Dose, Mg. per Gm.	*Rana pipiens.* No. of Hearts in Systole/No. of Frogs Used.	*Bufo valliceps.* Dose, Mg. per Gm.	*Bufo valliceps.* No. of Hearts in Systole/No. of Toads Used.	Ratio of *R. pipiens* to *B. valliceps.*
Ouabain-Merck	0.00050	0/4	0.03000	0/4	
	0.00055	0/4	0.04000	1/4	
	0.00060	1/4	0.04500	0/4	1:77
	0.00065	4/4	*0.05000*	3/4	
			0.05500	3/4	
Cymarin	0.00035	0/4	0.05500	0/4	
	0.00040	0/4	0.07500	0/4	
	0.00045	0/4	0.15000	0/4	
	0.00050	0/4	0.30000	0/1	
	0.00055	0/4	0.40000	0/1	1:167
	0.00060	3/4	0.60000	0/2	
	0.00065	3/4	0.80000	0/4	
	0.00070	4/4	1.00000	0/4	
	0.00075	4/4	*1.10000*	4/4	
			1.20000	4/4	
Coumingine Hydrochloride	0.00200	0/4	0.10000	0/1	
	0.00250	2/8	0.12500	0/1	
	0.00300	6/8	0.15000	3/7	
	0.00300	4/4	*0.17500*	4/7	1:58
	0.00750	4/4	0.20000	5/5	
	0.01000	4/4	0.22000	4/4	

The results are summarized in Table I. It may be noted that the minimal systolic dose of cymarin in frogs is 0.0006 mg. per Gm., and that in toads 1.1 mg. per Gm. The ratio of sensitivity between frogs and toads is therefore 1:167. Similarly, the minimal systolic dose of coumingine hydrochloride in frogs is 0.003 mg. per Gm., and that in toads 0.175 mg. per Gm. The ratio of sensitivity between frogs and toads in this case is 1:58. It may be pointed out here that the figures for the frogs in Table I are larger than those reported previously (2), (3). This is due to the fact that different batches of frogs respond differently to ouabain, that is, the minimal systolic dose may vary from time to time. In order to make

accurate comparisons of various cardiac principles in frogs, it has been our custom to recalculate the dose by proportion as if every batch of frogs has the same minimal systolic dose to ouabain, namely, 0.0005 mg. per Gm. In the present work no such correction was made because the main point of interest was to find the difference of sensitivity between frogs and toads.

In the previous paper (1), it was shown that the toad was 150 times more tolerant to *G*-strophanthin than the frog. The ratio was redetermined with a new lot of ouabain-Merck (*G*-strophanthin), and it was found, as shown in Table I, to be 1:77, practically one-half of the former figure. It is difficult to account for the discrepancy of results at present, except to mention that the former tests were carried out in the fall, and the present ones in the spring although both were made at 20° C.

SUMMARY.

The nebulous toad, *Bufo valliceps*, has a natural tolerance to cardiac glycosides as well as alkaloids. When compared with the common frog, *Rana pipiens*, it is 167 times less sensitive to cymarin, and 58 times less sensitive to coumingine hydrochloride. In the present investigation it is also found that the ratio of susceptibility to ouabain between the same species of the frog and the toad is 1:77 as contrasted with that of 1:150 reported previously.

REFERENCES.

(1) Chen, K. K., and Chen, A. L., *J. Pharmacol.*, 47, 295 (1933).
(2) Chen, K. K., Chen, A. L., and Anderson, R. C., JOUR. A. PH. A., 25, 579 (1936).
(3) Chen, K. K., Hargreaves, C. C., and Winchester, W. T., *Ibid.*, 27, 9 (1938).
(4) Pharmacopœia of the United States, XI Revision, Mack Printing Co., Easton, Pa., 397 (1936).

DIGITALIS ASSAY BY THE CAT METHOD UNDER "SODIUM AMYTAL" ANESTHESIA.*

BY WILLIAM E. FRY AND EDWARD E. SWANSON.[1]

In the assay of digitalis by the Hatcher-Brody Cat Method (1), the question of anesthesia has been a problem of much discussion. Rowe (2) and Chopra and Chowhan (3) suggested the substitution of chlorobutanol in place of ether, assuming that this would not affect the size of the cat unit. Epstein (4) found that paraldehyde lowered the resistance of the cat to digitalis. With ether, chlorobutanol, urethane, chloralose and paraldehyde, David and Rajaminchan (5) observed that the choice of anesthetic was of much importance in the results of the cat unit. Haskell (6) noted a larger cat unit with dial-urethane anesthesia. With urethane, Edmunds, Moyer and Shaw (7) reported more of an increase in the cat unit for the U. S. P. Standard Powder than with ether, and concluded that the effect of anesthetics has a marked influence upon the amount of digitalis in the cat unit. Bauer and Fromherz (8) in the assay of ouabain obtained a larger cat unit with allylisopropyl barbituric acid than with ether.

EXPERIMENTAL.

In the present work, experiments were carried out with two short-acting barbituric acid derivatives as anesthetics. The compounds used were "Sodium Amytal" (Sodium Iso-amyl

* Scientific Section, A. PH. A., New York meeting, 1937.

[1] Eli Lilly & Co., Research Laboratories.

Ethyl Barbiturate, Lilly) and "Seconal" (Sodium Propyl-methyl-carbinyl Allyl Barbiturate, Lilly). As previously reported (9), (10), (11), "Seconal" has a smaller minimal anesthetic dose (M. A. D.), a smaller minimal lethal dose (M. L. D.), and a distinctly shorter duration of action than "Sodium Amytal." In cats, intraperitoneally, the M. A. D. was 70 mg. per Kg. for "Sodium Amytal" and 35 mg. per Kg. for "Seconal."

The digitalis preparations used in these experiments were the U. S. P. Standard Digitalis Powder and two tinctures of digitalis U. S. P. With each preparation, not less than forty-eight cats were used, sixteen under ether and sixteen under each of the barbituric acid compounds. All females were non-pregnant and non-lactating. The barbituric acid derivatives were injected intraperitoneally. In each experiment the blood pressure was recorded.

As shown in Table I, and summarized in Table II, under ether anesthesia the average fatal dose of a 10 per cent solution of the U. S. P. Standard Digitalis Powder is 0.0558 Gm. per Kg. With "Seconal" anesthesia, the U. S. P. Standard has an average fatal dose of 0.0685 Gm. per Kg. as against 0.0777 Gm. per Kg. under "Sodium Amytal" anesthesia.

TABLE I.—COMPARISON OF TWO BARBITURIC ACID DERIVATIVES WITH ETHER IN THE DIGITALIS ASSAY IN CATS.

Drug	Anesthetic. Ether. Cat No.	Sex.	Weight. Kg.	Fatal Dose. Gm. per Kg.	"Seconal." Cat No.	Sex.	Weight. Kg.	Fatal Dose. Gm. per Kg.	"Sodium Amytal." Cat No.	Sex.	Weight. Kg.	Fatal Dose. Gm. per Kg.
U. S. P. Standard Powder Digitalis, 10% Solution in 80% Alcohol.	201	F	1.738	0.0587	217	F	2.475	0.0715	233	F	1.950	0.0815
	202	F	1.828	0.0459	218	F	2.010	0.0896	234	F	1.979	0.0879
	203	F	1.787	0.0520	219	F	2.000	0.0810	235	F	1.856	0.0792
	204	F	2.300	0.0509	220	F	1.710	0.0509	236	F	2.270	0.0687
	205	F	2.167	0.0581	221	F	2.320	0.0582	237	F	2.222	0.0810
	206	F	1.885	0.0597	222	F	2.495	0.0643	238	F	1.946	0.0748
	207	F	2.310	0.0591	223	F	2.068	0.0689	239	F	1.820	0.0808
	208	F	2.310	0.0526	224	F	2.168	0.0747	240	F	1.900	0.0726
	209	M	2.137	0.0660	225	M	2.780	0.0680	241	M	2.455	0.0733
	210	M	2.585	0.0441	226	M	2.212	0.0854	242	M	2.664	0.0698
	211	M	2.451	0.0575	227	M	2.487	0.0784	243	M	2.563	0.0720
	212	M	2.820	0.0691	228	M	2.535	0.0615	244	M	1.956	0.0840
	213	M	2.556	0.0528	229	M	2.496	0.0553	245	M	1.908	0.0849
	214	M	2.091	0.0545	230	M	2.393	0.0577	246	M	2.773	0.0800
	215	M	1.971	0.0533	231	M	2.591	0.0533	247	M	2.220	0.0831
	216	M	2.328	0.0586	232	M	2.559	0.0668	248	M	2.535	0.0704
			Average	0.0558			Average	0.0685			Average	0.0777
Tincture Digitalis U. S. P. A.	249	F	2.295	0.0497	265	F	1.820	0.0725	281	F	2.256	0.0718
	250	F	2.976	0.0489	266	F	1.839	0.0571	282	F	2.595	0.0566
	251	F	2.050	0.0644	267	F	2.155	0.0529	283	F	1.825	0.0986
	252	F	1.961	0.0474	268	F	2.281	0.0566	284	F	2.096	0.0558
	253	F	2.289	0.0472	269	F	1.955	0.0775	285	F	2.190	0.0657
	254	F	2.356	0.0420	270	F	2.197	0.0643	286	F	1.680	0.0786
	255	F	1.679	0.0608	271	F	2.119	0.0792	287	F	2.112	0.0625
	256	F	2.275	0.0527	272	F	2.545	0.0737	288	F	2.130	0.0662
	257	M	2.403	0.0449	273	M	2.169	0.0650	289	M	1.880	0.0798
	258	M	2.072	0.0637	274	M	2.581	0.0744	290	M	2.663	0.0676
	259	M	2.204	0.0408	275	M	2.058	0.0751	291	M	2.696	0.0612
	260	M	2.375	0.0559	276	M	2.640	0.0682	292	M	2.055	0.0788
	261	M	2.098	0.0536	277	M	2.720	0.0704	293	M	2.669	0.0539
	262	M	2.246	0.0628	278	M	2.910	0.0752	294	M	1.960	0.0627
	263	M	2.514	0.0596	279	M	1.805	0.0598	295	M	2.645	0.0749
	264	M	2.565	0.0456	280	M	2.098	0.0715	296	M	1.691	0.0798
			Average	0.0524			Average	0.0684			Average	0.0696

Tincture Digitalis U. S. P. B.

297	F	1.636	0.0623	313	F	2.128	0.0916	331	F	2.446	0.0944
298	F	1.922	0.0601	314	F	1.921	0.0734	332	F	2.095	0.0759
299	F	2.394	0.0514	315	F	2.720	0.0684	333	F	2.475	0.0715
300	F	1.803	0.0524	316	F	2.302	0.0730	334	F	2.024	0.0741
301	F	2.489	0.0596	317	F	2.720	0.0684	335	F	2.000	0.0750
302	F	1.912	0.0706	318	F	2.295	0.0680	336	F	2.915	0.0664
303	F	2.381	0.0623	319	F	2.172	0.0753	337	F	2.311	0.0753
304	F	2.404	0.0624	320	F	2.347	0.0575	338	F	1.980	0.0818
305	M	1.785	0.0504	321	M	2.491	0.0915	339	M	2.754	0.0980
306	M	2.776	0.0567	322	M	2.041	0.0661	340	M	2.125	0.0918
307	M	2.399	0.0714	323	M	1.976	0.0760	341	M	1.748	0.0971
308	M	2.300	0.0620	324	M	2.842	0.0855	342	M	2.704	0.0739
309	M	2.248	0.0647	325	M	2.052	0.0935	343	M	2.435	0.1041
310	M	2.263	0.0497	326	M	2.993	0.0631	344	M	2.510	0.0705
311	M	2.774	0.0595	327	M	1.817	0.1024	345	M	2.888	0.0727
312	M	2.067	0.0581	328	M	2.488	0.0687	346	M	2.843	0.0971
...	..	...	....	329	M	1.891	0.0872	...	..	...	....
...	..	...	....	330	M	2.365	0.0749	...	..	...	....
		Average	0.0596			Average	0.0764			Average	0.0824

TABLE II.—SUMMARY OF RESULTS.

Digitalis.	Ether. Average Fatal Dose. Gm. per Kg.	"Seconal" Average Fatal Dose. Gm. per Kg.	"Seconal" Difference between "Seconal" and Ether. Gm. per Kg.	Anesthetic. Increase over Ether. Per Cent.	"Sodium Amytal." Average Fatal Dose. Gm. per Kg.	"Sodium Amytal." Difference between "Sodium Amytal" and Ether. Gm. per Kg.	"Sodium Amytal." Increase over Ether Per Cent.
U. S. P. Standard Powder	0.0558	0.0685	0.0127	22.7	0.0777	0.0219	39.0
Tincture A	0.0524	0.0684	0.0160	30.5	0.0696	0.0172	32.8
Tincture B	0.0596	0.0764	0.0168	28.3	0.0824	0.0228	38.2

For the tincture of digitalis U. S. P. sample A, the average fatal dose under ether anesthesia is 0.0524 Gm. per Kg. With "Seconal" anesthesia, the average fatal dose is 0.0684 Gm. per Kg. With the same tincture under "Sodium Amytal," the average fatal dose is 0.0696 Gm. per Kg.

The tincture of digitalis U. S. P. sample B under ether anesthesia has an average fatal dose of 0.0596 Gm. per Kg. With "Seconal" and "Sodium Amytal" anesthesia, the average fatal doses are 0.0764 and 0.0824 Gm. per Kg., respectively.

As summarized in Table II, under "Seconal" anesthesia, it required 0.0127 Gm. per Kg. (22.7 per cent) more of the U. S. P. Standard Digitalis Powder than when ether was used, and 0.0219 Gm. per Kg. (39 per cent) more under "Sodium Amytal" anesthesia. For tincture A, with "Seconal" anesthesia, 0.0160 Gm. per Kg. (30.5 per cent) more was necessary to cause death and 0.0172 Gm. per Kg. (38.2 per cent) more with "Sodium Amytal" than under ether anesthesia. Sample B tincture with "Seconal" and "Sodium Amytal" anesthesia required 0.0168 Gm. per Kg. (28.3 per cent) and 0.0218 Gm. per Kg. (38.2 per cent) more, respectively, than when ether was used. Thus, both barbituric acid derivatives, more marked with "Sodium Amytal" than with "Seconal," increased the amount of digitalis required to kill more than ether, or the size of the cat unit depends upon the anesthetic employed.

CONCLUSIONS.

(1) As anesthetics, in the assay of digitalis by the cat method, two short-acting barbituric acid derivatives were compared with ether.

(2) When the cats were anesthetized with the barbituric acid compounds, it required more digitalis to kill than with ether.

(3) The size of the cat unit for digitalis varies with the anesthetic agent used.

REFERENCES.

(1) Hatcher and Brody, *Am. J. Pharm.*, 82 (1910).
(2) Rowe, JOUR. A. PH. A., 8, 900 (1919).
(3) Chopra and Chowhan, *Indian J. Med. Research*, 20, 1189 (1932–1933).
(4) Epstein, *Quart. J. Pharm. & Pharmacol.*, 6, 169 (1933).
(5) David and Rajaminichan, *Ibid.*, 7, 36 (1934).
(6) Haskell, *J. Pharmacol. & Exper. Therap.*, 58, 111 (1936).
(7) Edmunds, Moyer and Shaw, JOUR. A. PH. A., 26, 290 (1937).
(8) Bauer and Fromherz, *Arch. exptl. Path. Pharmakol.*, 172, 693 (1933).
(9) Swanson and Shonle, *J. Pharmacol. & Exper. Therap.*, 41, 289 (1931).
(10) Swanson, *Proc. Soc. Exptl. Biol. Med.*, 32, 1563 (1935).
(11) Swanson and Fry, JOUR. A. PH. A., 26, 1248 (1937).

A CRITICAL STUDY OF THE TANNIN-BEARING GALENICALS.*[1]

BY S. W. ARNETT[2] AND C. O. LEE.[3]

This study was undertaken for the purpose of finding answers to several problems which have been raised concerning the official tannin-bearing galenicals. The objectives for this investigation briefly were as follows:

1. To determine the effects of the changes in menstrua, as specified in the recent revisions of the United States Pharmacopœia and National Formulary, upon the permanency, astringency and total extractive of the official tannin-bearing galenicals.

2. To determine the effect of precipitation upon the astringency of these galenicals.

3. To find out whether there is any correlation between the astringency, total extractive and precipitation in such preparations.

4. To determine whether precipitation in such galenicals can be prevented by the use of selective menstrua or other means.

5. Most important of all, perhaps, to determine whether these products can be reliably assayed for tannin.

THE ESTIMATION OF THE PRECIPITATE.

The sixteen galenicals which were studied are given in Table I and are arranged in the increasing order of the weights of their precipitates. The amounts shown here were obtained from 50-cc. sealed ampul samples of each of the preparations which had stood for five months. At the end of this period the ampuls were opened, the precipitate collected in Gooch crucibles and dried to constant weight.

An attempt was made to estimate the relative amounts of precipitates which formed in these preparations by examining liter portions of them after they had stood in Erlenmeyer flasks for about four months. Variations in the densities, and other physical differences in the precipitates, makes such readings difficult, especially when so many different drugs are involved.

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[2] National Formulary Fellow, of the AMERICAN PHARMACEUTICAL ASSOCIATION, 1936–1937.

[3] Professor of Pharmacy, Purdue University, School of Pharmacy.

TABLE I.

Galenical.	Process.	Weight of Precipitate in Gm.
Tincture of Krameria	Special	0.0011 Gm.
Tincture of Kino	U. S. P. XI	0.0034 Gm.
Tincture of Krameria	U. S. P. X	0.0064 Gm.
Tincture of Nutgall	N. F. VI	0.0129 Gm.
Compound Tincture of Gambir	U. S. P. X	0.0134 Gm.
Tincture of Kino	U. S. P. X	0.0226 Gm.
Fluidextract of Hamamelis Leaves	N. F. V	0.0268 Gm.
Compound Tincture of Gambir	N. F. VI	0.0442 Gm.
Fluidextract of Krameria	N. F. VI	0.0466 Gm.
Fluidextract of Krameria	N. F. V	0.0466 Gm.
Fluidextract of Hamamelis Leaves	N. F. VI	0.0543 Gm.
Fluidextract of Castanea	N. F. V	0.0610 Gm.
Fluidextract of Castanea	N. F. VI	0.1051 Gm.
Fluidextract of Rose	N. F. VI	0.1221 Gm.
Fluidextract of Uva Ursi	N. F. VI	0.1574 Gm.
Fluidextract of Uva Ursi	U. S. P. X	0.2191 Gm.

COMMENTS CONCERNING THE PREPARATIONS.

Compound Tincture of Gambir.—The preparation official in the U. S. P. X provided a stable product in which slight precipitation occurred. The N. F. VI galenical precipitated badly. It should be stated that the latter formula specifies four times the amount of drug for extraction as does the U. S. P. X formula.

The N. F. VI tincture precipitates immediately after the percolation is completed and continues at a decreasing rate for an indefinite period of time. The deposit appears to be crystalline by macroscopic observation but gives no evidence of a definite structure under the microscope.

Tincture of Kino.—The U. S. P. XI product is an improvement over the one formerly official inasmuch as it is more stable, more limpid, and less liable to gelatinization.

Fluidextract of Hamamelis Leaves.—There is no question but that the new official product is superior from the standpoint of stability.

Fluidextract of Castanea.—There were more notable improvements manifested in the N. F. VI product over the N. F. V preparation than in any other galenical under consideration. The amount of precipitate was greatly reduced in the new official fluidextract.

Tincture of Krameria.—This galenical was unquestionably the most suitable preparation from the standpoint of stability. The tincture official in the U. S. P. X gave evidence of only a trace of sediment. The Tincture of Krameria Special (made according to the directions specified for Tincture of Kino U. S. P. XI) was the only tincture entirely free from sediment at the conclusion of this investigation.

From the point of view of stability, Tincture of Krameria Special proved to be the most desirable astringent galenical in this group.

Tincture of Nutgall.—Precipitation began in this tincture before the percolation was complete. The precipitation appears to be rather complete after a month or two of standing after which time there is little additional sedimentation. This galenical does not precipitate badly but tends to darken considerably upon standing.

Fluidextract of Rose.—The deposit of a precipitate in this galenical does not occur immediately upon the completion of the product and makes its appearance very gradually. The fluidextract is very viscous which may, in part, account for this.

Fluidextract of Krameria.—Here again the N. F. VI product shows marked improvement over the one formerly official in the N. F. V. The new official product was the only fluidextract under observation which showed no tendency toward sedimentation. The N. F. VI fluidextract is a more limpid fluid and has the general property of an improved physical appearance.

Fluidextract of Uva Ursi.—The N. F. VI galenical gave no visible signs of improvement over the U. S. P. X product. Both fluidextracts precipitated badly upon standing. The precipitate when examined under the microscope proved to be non-homogenous in nature and showed the presence of a distinct crystalline structure which has been identified as ellagic acid by Parks (17). This was the only precipitate that was definitely crystalline in structure. There was also present a large amount of amorphous matter in the precipitate.

DETERMINATION OF TOTAL EXTRACTIVE IN THE TANNIN-BEARING GALENICALS.

Total extractive determinations were made upon the sixteen galenicals immediately upon the completion of their manufacture, again after one month had elapsed, and a final determination at the completion of the investigation which represented a period of three to five months.

The procedure employed in making these total extractive determinations is as follows: Ten milliliters of the galenical were carefully pipetted on to a four-inch watch glass and the pipette allowed to drain until dropping had ceased. The watch glass was then placed in an electric oven and dried to constant weight at 105°. The weight of the residue multiplied by ten equals the percentage of total extractive, weight/volume. The results are shown in Table II.

TABLE II.—TOTAL EXTRACTIVES (PERCENTAGE, WEIGHT/VOLUME).

Galenical.	Determination. First.	Second.	Final.
Compound Tincture of Gambir, U. S. P. X	5.1	5.0	5.1
Compound Tincture of Gambir, N. F. VI	15.3	20.2	19.7
Tincture of Kino, U. S. P. X	13.7	14.0	14.9
Fluidextract of Hamamelis Leaves, N. F. V	22.7	22.7	23.4
Tincture of Kino, U. S. P. XI	10.2	9.2	9.8
Fluidextract of Hamamelis Leaves, N. F. VI	10.3	11.5	11.3
Fluidextract of Castanea, N. F. V	15.9	15.4	15.1
Fluidextract of Castanea, N. F. VI	15.1	15.6	15.7
Tincture of Krameria, U. S. P. X	7.1	7.1	6.8
Tincture of Krameria, Special	8.6	8.4	7.7
Tincture of Nutgall, N. F. VI	10.2	9.5	9.5
Fluidextract of Rose, N. F. VI	34.4	41.4	42.3
Fluidextract of Krameria, N. F. V	33.5	33.6	33.7
Fluidextract of Krameria, N. F. VI	35.7	33.8	32.4
Fluidextract of Uva Ursi, U. S. P. X	37.9	36.9	36.3
Fluidextract of Uva Ursi, N. F. VI	35.2	35.1	33.5

Comments.—It was hoped that the increased alcoholic strength of the menstrua and solvents might cause a reduction in the amount of total extractive in these galenicals without appreciably affecting the astringency. Fluidextract of Hamamelis Leaves was the only preparation to show any marked improvement of this sort. Its total extractive dropped about 50% while its tannin content increased materially.

There was little noticeable change in the total extractives of the other preparations. Compound Tincture of Gambir was the only one to give any evidence of an

increased amount of extractive. This would be expected because the strength of the N. F. VI galenical is four times that of the U. S. P. X.

The fluidextracts of Rose, Krameria and Uva Ursi have maintained their high extractive content.

THE ESTIMATION OF TANNIN.

A modification of the Lowenthal Method of tannin analysis was used for the determination of tannin in this study (14). The method involves permanganate titration and gelatin precipitation.

Preliminary to applying the assay to the galenicals, a series of ten tannin solutions were prepared and assayed. Water was the solvent for one, a solution of alcohol 9 and glycerin 1 being the solvent for the other nine solutions. To seven of these reasonable amounts of presumably interfering substances were added. These were, gallic acid, resorcinol, resin, cholesterol, sucrose, glucose and chlorophyll. These solutions were assayed when freshly prepared, again at the end of ten days, and the third time at the end of twenty-four days.

From the results obtained it was concluded that tannin can be assayed reliably and reproducibly within about 1%. It was also shown that these tannin solutions are reasonably stable and that the substances added did not interfere with the tannin analysis.

The galenicals under study were each assayed five times by the method which has been mentioned. The intervals and results of these are shown in Table III.

TABLE III.

Galenical.	Process.	At Time of Completion.	After 10 Days.	After 20 Days.	After 30 Days.	Final 3–5 Months.
Compound Tincture of Gambir						
	U. S. P. X	1.0	1.3	1.6	1.7	2.0
	N. F. VI	2.8	2.8	2.4	5.6	5.8
Tincture of Kino						
	U. S. P. X	8.3	8.5	9.4	8.6	8.5
	U. S. P. XI	5.2	6.0	5.6	5.3	5.2
Fluidextract of Hamamelis Leaves						
	N. F. V	1.9	2.9	2.3	2.3	3.0
	N. F. VI	4.2	3.8	4.3	3.4	3.6
Fluidextract of Castanea						
	N. F. V	1.0	1.1	0.9	0.9	1.0
	N. F. VI	1.7	1.9	1.7	1.4	1.2
Tincture of Krameria						
	U. S. P. X	3.6	3.3	3.1	2.7	2.8
	Special	2.9	2.9	2.9	2.4	2.9
Tincture of Nutgall						
	N. F. VI	7.3	6.9	6.6	7.6	7.1
Fluidextract of Rose						
	N. F. VI	9.1	11.2	13.7	13.5	11.7
Fluidextract of Krameria						
	N. F. V	7.5	9.2	12.5	11.5	12.0
	N. F. VI	7.2	6.8	9.9	9.6	9.9
Fluidextract of Uva Ursi						
	U. S. P. X	7.43	6.6	7.1	6.7	6.7
	N. F. VI	6.2	6.8	9.5	9.6	8.6

COMMENTS UPON THE ESTIMATION OF TANNIN IN THE GALENICAL PREPARATIONS.

The value of any definite conclusions which might be drawn from the information tabulated in Table III is problematical. Reliable results seem to be evident in the instances of Tincture of Nutgall, Tincture of Krameria, Tincture of Kino, Fluidextract of Hamamelis Leaves and Fluidextract of Castanea. The galenicals, possessing high total extractive, namely: Fluidextract of Rose, Fluidextract of Krameria and Fluidextract of Uva Ursi, did not give concordant assay values. They showed a tendency toward increased permanganate values upon aging. Compound Tincture of Gambir also manifested this tendency.

Why these preparations showed an increase in tannin content remains an unsolved problem. This phenomenon cannot be explained upon the basis of evaporation of the highly volatile solvent. If such were the case, the occurrence would be common to all of the preparations. Neither can this discrepancy be attributed to faulty technique. It would seem that some of these preparations show a marked increase in permanganate value caused by some change within the galenical itself. It is difficult to say just what rôle the high total extractives play in the explanation of this definite trend toward increased tannin values.

It will be observed that there has been no marked decrease in the permanganate values, as would be expected if these preparations lost much of their astringency with age. If tannin were being thrown out as a part of the precipitate the assay should indicate it. Furthermore, it would seem that the assay figures for the freshly prepared galenicals should represent their tannin content and astringency rather well.

ATTEMPTS AT REDUCING THE FORMATION OF PRECIPITATES.

In 1933 Ball (15) showed that the precipitate which appears in Fluidextract of Uva Ursi could be greatly diminished by subjecting the crude drug, previous to percolation, to the action of steam under pressure. Parks (17) in 1936 followed up the work of Ball. By subjecting the crude drug to steam under fifteen pounds of pressure for thirty minutes, he was able to obtain fluidextracts which remained virtually free from precipitates for indefinite periods of time. He attributed the cause of precipitation in this particular preparation to the action of enzymes which were rendered inactive by the heat treatment.

The crude drugs, which are indicated in Table IV, were placed in porcelain evaporating dishes and exposed to twenty pounds of steam pressure for one hour on one day only, then used to make their respective fluidextracts.

Tannin assays were made upon these preparations and compared to controls. The effect of the heat treatment, upon precipitation is also shown in the following table.

TABLE IV.

Galenical.	Tannin Assay. Autoclave Sample.	Control Sample.	Effect upon Precipitation.
Fluidextract of Rose	10.4%	9.8%	Decreased
Fluidextract of Hamamelis Leaves	3.8%	3.3%	Decreased
Fluidextract of Uva Ursi	7.7%	8.9%	Decreased
Fluidextract of Krameria	3.7%	3.8%	Undetermined

SUMMARY AND CONCLUSIONS.

1. The following galenicals, when made according to the new official formulas showed improvement as to permanency over those manufactured by the process formerly official:

(*a*) Tincture of Kino
(*b*) Fluidextract of Hamamelis Leaves
(*c*) Fluidextract of Castanea
(*d*) Fluidextract of Krameria

2. The U. S. P. X formula for Compound Tincture of Gambir provided a more stable galenical than the process now official in the N. F. VI. The marked increase in strength of the latter preparation probably explains this increased precipitation.

3. Tincture of Krameria, now non-official, provides a most desirable galenical if made by type process M using a menstruum of alcohol 9, glycerin 1 as solvent. No precipitation occurred in this preparation during four months' storage.

4. The Fluidextracts of Uva Ursi, Krameria and Rose contain a very high percentage of total extractive. This is objectionable from the standpoint of permanency.

5. Changes seem to occur in galenical preparations upon standing, especially those with high total extractive values. This change results in a marked increase of reducing substances.

6. An accurate assay for tannin in galenical preparations cannot be accomplished with any of the existing methods of analysis. This is not likely to be achieved until the chemistry of tannins is more fully understood and a method of isolation devised.

7. Precipitation in tannin-bearing galenicals does not seem to materially influence their astringency.

8. Autoclaving of the crude drug prior to the process of galenical manufacture, proved to be of definite value in reducing precipitation in the Fluidextracts of Rose, Uva Ursi, and Hamamelis Leaves.

9. Light is not an influencing factor in causing precipitation in the astringent galenicals.

REFERENCES.

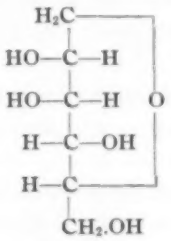
(1) Thayer, H., *Am. J. Pharm.*, 31, 216–222 (1859).
(2) Diehl, C. L., Proc. A. Ph. A., 26, 681–697 (1878).
(3) Procter, H. R., *Ibid.*, 26, 551–558 (1878).
(4) Lloyd, J. U., *Ibid.*, 29, 408–421 (1881).
(5) Small, F. H., *J. Soc. Chem. Ind.*, 25, 296–298 (1906).
(6) Scoville, W. L., Jour. A. Ph. A., 1, 334–337 (1912).
(7) Dott, D. B., *J. Soc. Chem. Ind.*, 34, 1124–1125 (1915).
(8) Jordan, C. J., and Ware, A. H., *Pharm. J.*, 113, 102 (1924).
(9) Forbes, W. B., *Ibid.*, 116, 225 (1926).
(10) Nierenstein, M., *Ibid.*, 116, 287 (1926).
(11) Scoville, W. L., Jour. A. Ph. A., 16, 1136–1146 (1927).
(12) Jones, A. E., *Analyst*, 52, 275 (1927).
(13) Nierenstein, M., "Allen's Commercial Organic Analysis," 5, 78 (1927).
(14) "A. O. A. C. Official Methods of Analysis" (1930), page 155.
(15) Ball, J. E., "Unpublished Thesis," Purdue University (1933).
(16) Nierenstein, M., The Natural Organic Tannins (1935).
(17) Parks, L. M., Unpublished Thesis, Purdue University (1936).

SUGAR ALCOHOLS XIV.

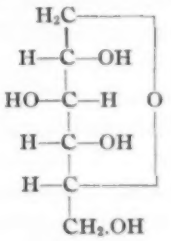
THE ISOLATION OF POLYGALITOL FROM *POLYGALA SENEGA* AND THE PHYSICOCHEMICAL AND BIOLOGICAL PROPERTIES OF POLYGALITOL.*

BY C. JELLEFF CARR AND JOHN C. KRANTZ, JR.[1]

Polygalitol has been isolated from the leaves and stems of *P. Amara* by Chodat (1), from *P. vulgaris* by Picard (2) and from *P. Tennuifolia* by Shinoda, Sato and Sato (3). This anhydride was extracted from the fresh plants as a white crystalline compound m. p. 142–143° C., $[\alpha]_D^{16} = +47.81°$. Polygalitol has been shown to have the following formula and is isomeric with styracitol synthesized from glucose. Both compounds yield the same glucosazone m. p. 208° C. (4).[2]



Polygalitol



Styracitol

During the preparation of polygalitol in this laboratory in large quantities for animal experiments an improved method of isolation was developed. Since European species were difficult to obtain, it was of some interest to try local varieties of polygala. *Polygala Senega*, senega snakeroot, was selected because as an official drug it was more readily available. Price (5) has reported a sugar-like substance in extracts of senega root that he did not identify. In 1894 Guillaume-Gentil (6) reported a substance which he had obtained from *P. Senega* having a m. p. of 138° C. and suggested that it was similar to the "sugar" Chodat had isolated from the leaves of *P. Amara* six years before. In 1896 Schraeder (7) found sucrose in the root of *P. Senega* to the extent of 5 per cent and reported the presence of a small amount of sweet impure crystals in his preparation that he was unable to identify. Kain in 1898 (8) in Germany and Bienfang in this country in 1934 (9) also have reported sucrose as a constituent of senega root. Procter in 1860 (10) undoubtedly isolated a small amount of polygalitol from extracts of *P. Senega* although he did not report the physical properties. Since the roots only were used in these experiments, the leaves and stem as well as the root were used in this investigation. Jacobs and Isler (11) have recently made an exhaustive study of the sapogenins of *P. Senega* root.

EXPERIMENTAL.

1. Fresh Plant.—About 150 Gm. of fresh plant collected in the vicinity of Oakland, Md., on June 19, 1937, and identified pharmacognostically by Dr. Joseph E. Harned, were placed im-

* Scientific Section, A. PH. A., New York meeting, 1937.

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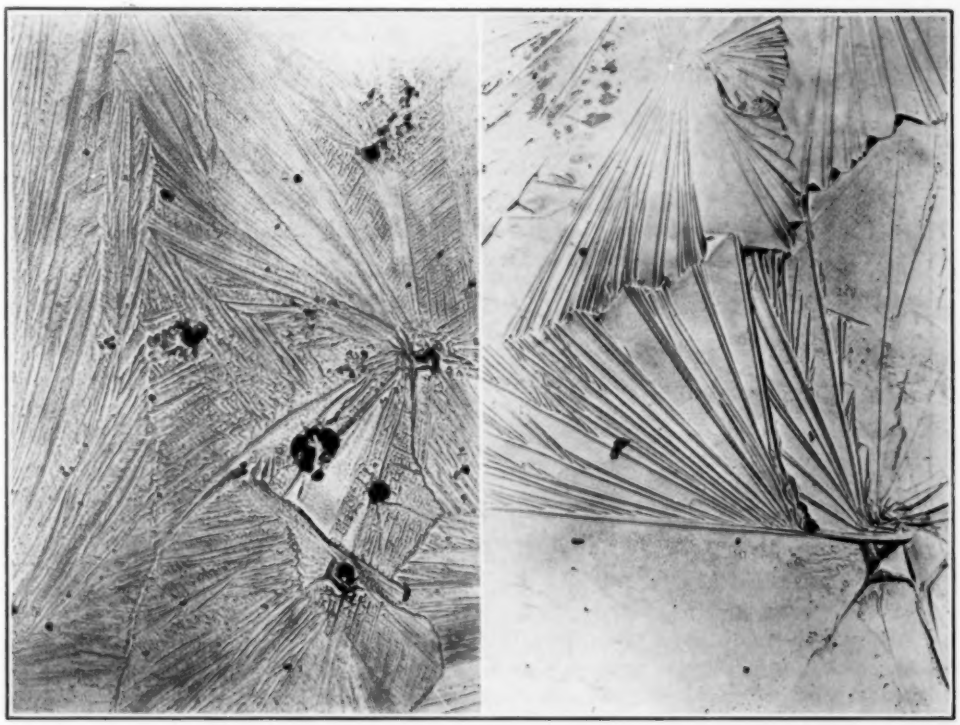
[2] Since this paper was submitted for publication Freudenberg and Rogers (*J. A. C. S.*, 59, 1602 (1937) have reported polygalitol as 1–5 anhydrosorbitol and styracitol, 1–5 anhydromannitol. These authors also were able to isolate 2 2 Gm. of crude polygalitol from dried *P. Senega*.

mediately in two liters of alcohol. The whole flowering plants deprived of their roots were used. After 36 hours the alcohol was recovered in a vacuum at low temperature until a light brown syrup remained. The syrup was dissolved in 100 cc. of water and lead subacetate was added until no further precipitation occurred, it was filtered and the excess lead was removed as sulfide. The clear lead-free filtrate was evaporated under reduced pressure to a syrup and was vigorously extracted with a mixture of 70 per cent ether in alcohol, filtered and evaporated to dryness. After standing in a desiccator for a week crystals of polygalitol formed as characteristic feathery rosettes. The crystals were purified by dissolving in water, adding charcoal, filtering and evaporating on a water-bath. Approximately 3 Gm. of impure crystals were obtained, which yielded 2 Gm. of pure polygalitol, m. p. 142–143° C. $[\alpha]_D^{16} + 47.3°$

2. *Dried Root.*—One pound of dried, powdered senega root from commercial sources was extracted with 50 per cent boiling alcohol until exhausted and the percolate evaporated and extracted



Crystals from *P. Senega.* Crystals from *P. Amara.*

Plate I.

as before. The alcohol-soluble fractions, after repeated purification with the ether-alcohol mixture and charcoal, yielded a colorless syrup which crystallized upon long standing in a desiccator. This product after recrystallization gave the characteristic melting point for polygalitol. Approximately 1 Gm. of pure compound was obtained. Plate I shows the characteristic feathery crystals of polygalitol from alcohol obtained from *P. Amara* and *P. Senega*. Armstrong has pointed out that the appearance of a 1–5 oxide ring in the alcohols is of interest, possibly indicating an intermediate stage in the synthesis of sugar alcohol from glucose (4).

Chodat in isolating polygalitol in 1888 reported the compound as an aldose which reduced Fehling's solution. Later Picard showed that the sugar alcohol he had isolated from *P. vulgaris* was identical with Chodat's compound. In these studies we have found a 70 per cent ether-alcohol mixture invaluable in removing traces of a reducing sugar-like substance that prevents complete purification. This material undoubtedly was the substance that led Chodat to believe polygalitol to possess a reducing group.

The yield of polygalitol reported by other workers varies from 0.85 to 2.2 per cent of air-dried plants deprived of their roots. Our yields have varied from 0.67 to 3.5 per cent of air-dried *P. Amara*, later methods of extraction yielding the higher value.

PHYSICOCHEMICAL PROPERTIES OF POLYGALITOL.

Polygalitol possesses a pleasant sweet taste which is followed by a very weak bitter taste. Repeated recrystallization failed to remove the bitter taste. The relative sweetness of polygalitol has been studied along with other sugar alcohols and certain of their anhydrides and previously reported (12). Polygalitol is the only anhydride of mannitol that possesses a sweet taste. The relative sweetness is in the ratio of 75 to 100, sucrose having an assigned value of 100, *d*-mannitol was found to possess a value of 57. The removal of water from a sugar alcohol with the formation

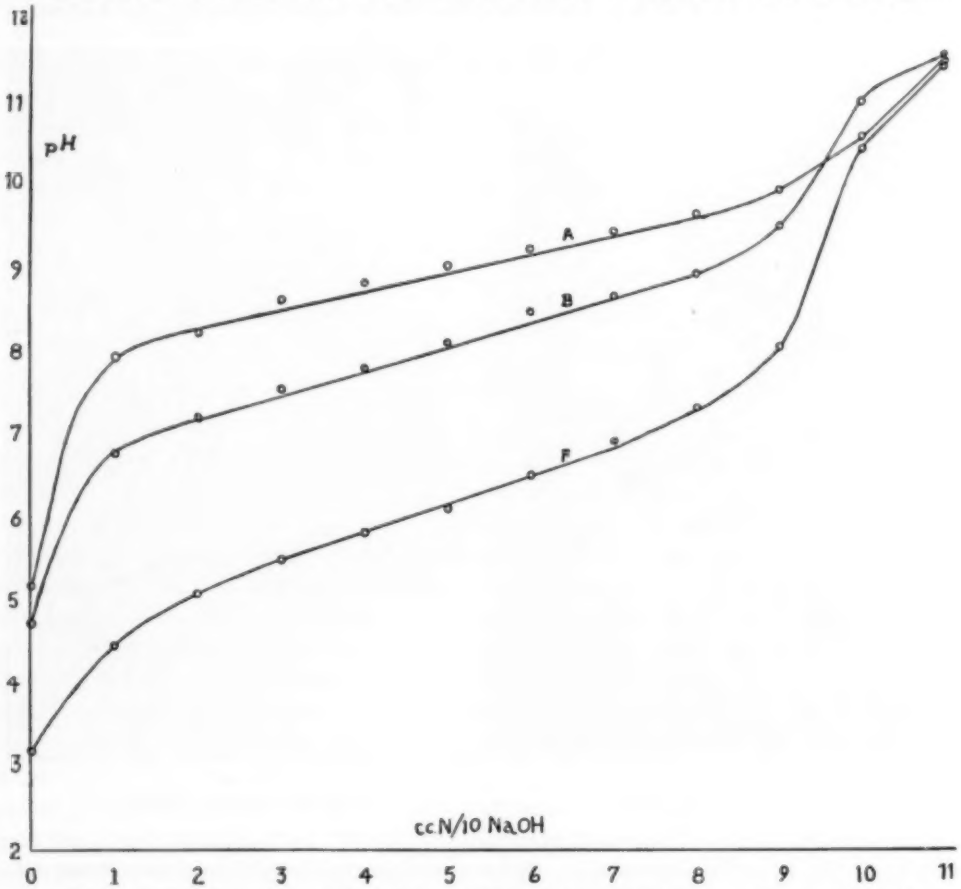


Fig. 1.—The effect of sugar alcohols on the dissociation of boric acid; Curve A, $M/10$ boric acid; curve B, $M/10$ boric acid + 4 per cent Mannitan or Glycerol; curve F, $M/10$ boric acid + 4 per cent Mannitol. The addition of 4 per cent Polygalitol to $M/10$ boric acid gives a curve approximating A.

of the anhydride as a rule destroys the sweet taste of the former. Polygalitol does not reduce Fehling's solution before or after hydrolysis. Upon ignition the compound yielded 0.87 per cent ash. The p_H of a 4 per cent aqueous solution of polygalitol gave a value of 6.7. The effect of the sugar alcohols and their anhydrides on the dissociation of boric acid has been studied previously (13, 14). Chart I shows the effect of polygalitol and mannitol on the dissociation of boric acid. In general, the anhydrides of the sugar alcohols potentiate the dissociation of boric acid to a lesser degree than do the parent substances. Polygalitol conforms perfectly to this generalization.

BIOLOGICAL PROPERTIES OF POLYGALITOL.

In former communications the authors have presented studies on the metabolism of the sugar alcohols and certain of their anhydrides in the animal body (15, 16, 17). No reports have been found in the literature regarding the metabolism of polygalitol, although its isomer, styracitol, has been partially investigated (18). Accordingly the authors investigated this problem. The results are summarized in Table I. In general polygalitol resembles the other anhydrides of

TABLE I.—SUMMARY OF RESULTS.

Glycogen Storage in Livers and Tissues of Rats after Polygalitol Diet.

Number of Animals.	Average Gm. Polygalitol Consumed.	Liver Glycogen Per Cent Mean.	Tissue Glycogen Per Cent Mean.
11	1.9	0.18	0.08
8	Controls	0.18	0.05

Respiratory Quotients during Fasting and after Polygalitol.

	Number of Animals.	Gm. O_2 per 100 Gm. per Hr.	R. Q.
Fasting	27	0.179	0.732
Polygalitol	27	0.185	0.745

Influence of Polygalitol on Blood-Sugar Level of Rabbits.

Number of Animals.	Mg. per 100 Cc. Blood. Fasting.	1/2 Hr.	1 Hr.	2 Hr.s	3 Hr.s	4 Hrs.	5 Hrs.
4	103	121	110	115	119	105	114
Glucose control							
4	97	179	255	243	197		
Water control							
2	88	101	112	114	125		

Influence of Polygalitol in Insulin Shock in Mice.

Number of Animals.	Hrs. Fasting.	Units per 100 Gm. Mouse.	Cc. 15 Per Cent Sol.	Recovery.
19 (Polygalitol)	12	5	1.4 to 4	None
20 (Glucose)	12	5	1.5	18

mannitol in that the white rat is incapable of storing glycogen or utilizing the compound as a carbohydrate to elevate the fasting respiratory quotient. Polygalitol is also without influence on the fasting blood-sugar level of the rabbit and is incapable of relieving the convulsions of insulin hypoglycemia. The details of these experiments will be published elsewhere.

The utilization of the sugar alcohols and their anhydrides by various microorganisms has been investigated (19). A study of these results compared with our previous findings reveals the interesting fact that although neither acid nor gas was formed from the anhydrides of mannitol, *i. e.*, mannitan, mannide, isomannide, both acid and gas were produced from the 1–5 anhydride, polygalitol. This sweet-tasting anhydride stands as an exception to the generalization that the removal of a molecule of water from the sugar alcohol molecule prevents their utilization by many organisms.

CONCLUSIONS.

1. Polygalitol, the 1–5 anhydride of mannitol, has been isolated from the fresh leaves and stem and from the dried root of *Polygala Senega* in pure form.

2. This anhydride occurs in the fresh flowering plant to the extent of approximately 2 per cent. Calculated on the basis of air-dried plant this concentration is considerably higher than that previously reported for other polygala species.

3. The discovery of this anhydride in other polygala species may be anticipated.

4. Polygalitol is one of the few anhydrides of the sugar alcohols that possesses a sweet taste.

5. Polygalitol, in accord with theory does not potentiate the dissociation of boric acid.

6. Polygalitol is not utilized as a carbohydrate in the animal body and in this respect resembles the other anhydrides of mannitol.

7. Certain bacteria possess the ability to utilize polygalitol with the production of acid and gas but are unable to utilize the other anhydrides of mannitol.

LITERATURE CITED.

(1) Chodat, M. R., *Arch. d. s. Phys. et Nat. Geneva*, 19, 290 (1888).
(2) Picard, M. P., *Bull. soc. chim. biol.*, 9, 692 (1927).
(3) Shinoda, J., Sato, S. and D., *Ber.*, 65, 1219 (1932).
(4) Armstrong, E. F., and Armstrong, K. F., "The Carbohydrates," Longmans, Green and Co., London (1934).
(5) Price, R., *Am. J. Pharm.*, 8, 92 (1937).
(6) Guillaume-Gentil, B., *Schweiz. Woch. Chem. Pharm.*, 32, 340 (1894).
(7) Schraeder, J. H., *Am. J. Pharm.*, 68, 178 (1896).
(8) Kain, J., *Pharm. Post*, 31, 61 (1898).
(9) Bienfang, R., JOUR. A. PH. A., 23, 396 (1934).
(10) Procter, Wm., *Am. J. Pharm.*, 32, 149 (1860).
(11) Jacobs, W. A., and Isler, O., *J. Biol. Chem.*, 119, 115 (1937).
(12) Carr, C. J., Beck, F. F., and Krantz, J. C., Jr., *J. A. C. S.*, 58, 1934 (1936).
(13) Krantz, J. C., Jr., Oakley, M., and Carr, C. J., *J. Phys. Chem.*, 40, 151 (1936).
(14) Krantz, J. C., Jr., Carr, C. J., and Beck, F. F., *Ibid.*, 40, 927 (1936).
(15) Carr, C. J., Musser, R., Schmidt, J., and Krantz, J. C., Jr., *J. Biol. Chem.*, 102, 721 (1933).
(16) Carr, C. J., and Krantz, J. C., Jr., *Ibid.*, 107, 371 (1934).
(17) Krantz, J. C., Jr., Evans, W. E., and Carr, C. J., *Quart. J. Pharm. Pharmacol.*, 8, 213 (1935).
(18) Freudenberg, W., *J. Biol. Chem.*, 99, 647 (1933).
(19) Dozois, K. P., Carr, C. J., and Krantz, J. C., Jr., *J. Bact.*, 32, 499 (1936).

RAPID CITY, SOUTH DAKOTA, OPENS HISTORICAL MUSEUM.

The Rapid City Historical Museum, Rapid City, South Dakota, was opened May 1st. Its field is Indian and pioneer material. The building is 134 by 41 feet, of native Minelusa limestone. The roof is supported entirely on the 18-inch walls, leaving the floor space unobstructed by structural elements. The cost was $30,000, of which two-thirds was furnished by the Works Progress Administration. The northern section houses the John A. Anderson collection of Indian material; the southern section includes space for the exhibition of pioneer material and an office for the custodian.

The AMERICAN PHARMACEUTICAL ASSOCIATION met in Rapid City in 1929.

OBSERVATIONS ON THREE LOUISIANA CAPSICUMS.

BY HEBER W. YOUNGKEN.[1]

During the past year the writer received specimens of the entire flowering and fruiting plants and dried fruits of a number of pungent red peppers grown at New Iberia and at Avery Island, La., for the purpose of making a botanical and pharmacognostic investigation to determine their identity, structure and their suitability as additional available sources of U. S. P. Capsicum.

Three of the more promising of these pungent peppers, namely, "Louisiana Long," "Louisiana Sport" and "Tabasco," which are used as spices, were first selected for study.

The purpose of this paper is to report his observations made upon these which include the study of the entire plants, fruits, seeds, sections of fruits and seeds, ground whole fruits, pungency tests, moisture, non-volatile extractive and ash.

CAPSICUM, LOUISIANA LONG.

This variety has been grown in Louisiana since about 1845 where it is known as "Long Cayenne" and "La. Longs." Its ground fruits have been used as a flavor especially for sausage and bologna.

Fig. 1.—*Capsicum annuum* L. var. *longum* Sendt., the source of Louisiana Long Capsicum. 1/6 ×.

Fig. 2.—Hybrid between Old Louisiana Sport Capsicum of Oriental origin and Honka variety of Japanese Capsicum, the source of the new Louisiana Sport Capsicum. 1/6 ×.

The plants studied were erect, frutescent, with greenish, often purple-striate branches and up to 3 ft. in height. The leaves were entire, ovate, petiolate, with acuminate apex, dark green, from 1 to 4 in. long and from 3/4 to 2.5 in. wide, with petioles sometimes exceeding the lamina. The flowers were large, white, with a 5-pointed, gamosepalous, pateriform calyx and spreading corolla. They were

[1] Laboratory of Pharmacognosy, Massachusetts College of Pharmacy.

borne solitary on curved or straight peduncles, the latter up to $1^1/_4$ in. in length and enlarging toward the calyx end. The fruits were red, oblong-conical, straight to frequently curved, up to 15 cm. in length and up to 2.5 cm. in breadth with pungent pericarp and seeds. (See Figs. 1 and 4*A*.)

The plants of this variety examined corresponded to the description by Irish (1) of *Capsicumannuum* L. **var.** *longum* Sendt. (2), and some of the specimens of fruits resembled Irish's figure of the Cardinal form of this variety in Pl. 13, Fig. 1 of his "Revision of the genus Capsicum." L. H. Bailey (3) in Gentes Herbarum regards this and other horticultural forms of Capsicum as forms of one species and calls this variety "*Capsicum frutescens* L. **var.** *longum* Sendt."

Description of Fruit.—Dried fruit oblong-conical, often curved, irregularly wrinkled, up to 15 cm. in length and up to 2.5 cm. in width, red to reddish brown,

Fig. 3.—*Capsicum annuum* Linné. **var.** *conoides* Irish, the source of Tabasco pepper. $^1/_6$ ×.

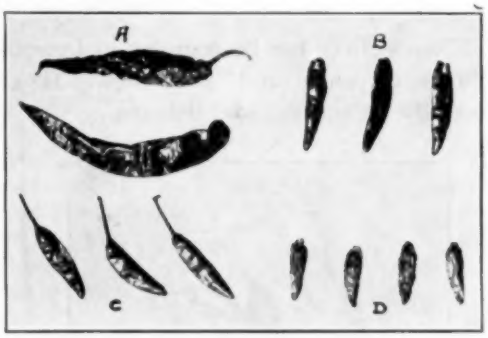


Fig. 4.—Four kinds of Louisiana grown pungent red peppers. *A*, La. Long; *B*, La. Sport; *C*, African Chillies × Japanese Capsicum (hybrid); *D*, Tabasco. $^1/_3$ ×.

2 to 3 celled; width of pericarp about 1 mm.; the calyx, when present, loosely enveloping the base, turbinate, gamosepalous, with a 5-toothed margin. Seeds flattened, sub-orbicular, albuminous, with a thick marginal ridge, up to 4 mm. in diameter; odor of crushed fruits aromatic; taste of pericarp very pungent and of seed, pungent.

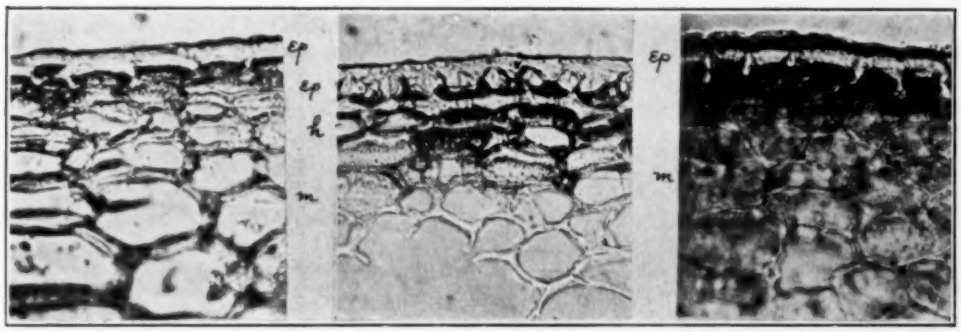
Histology.—(A) Pericarp. Transverse sections of the pericarp showed (1) an epicarp with cuticularized outer and radial walls, the latter frequently beaded or constricted, the cuticle of the outer walls being up to 19μ in thickness, the depth of the epicarp cells up to 38μ. (2) A mesocarp consisting of an outer region or hypodermis of somewhat collenchymatous cells, an inner broad region of thin-walled parenchyma containing red, orange and yellow chromoplastids and oil droplets and pervaded by bundles, and an inner layer of large giant cells. (3) An endocarp composed of a layer of stone cells and thin-walled, inner epidermal cells. Chromoplastids and oil droplets occurred in the outer epidermis, hypodermis, mesocarp parenchyma and endocarp. (See Figs. 5, 6 and 7*L*.)

Surface sections of the epicarp showed polygonal, quadrangular, to more rarely triangular epidermal cells with beaded, vertical walls, the latter up to about 11.4μ in thickness. The polygonal cells were sometimes elongated and from 38μ to 125μ in length and from 19μ to 45.6μ in width. Most of the epicarp cells had a large nucleus, a prominent nucleolus and orange to red chromoplastids and oil droplets.

(B) Seed. Transverse sections of the seed showed (1) a seed coat whose outer epidermis was composed of stone cells with extremely thick radial walls, the radial depth of some of the largest of these cells being up to 171μ, the outer walls of these being up to 38μ in thickness, (2) a broad endosperm of reserve parenchyma and (3) parts of a curved embryo. The endosperm cells appeared somewhat thinner walled than in the "Louisiana Sports" and "Tabasco" varieties.

Surface sections of the outer epidermis of the seed coat showed sinuate stone cells with greatly lignified and contorted walls, up to 332μ in length and with large pore canals.

Powdered Louisiana Long.—Red. Numerous fragments of large-celled parenchyma of mesocarp with thin cellulose walls and containing red to orange chromo-



L *S* *T*

Fig. 5.—Transverse sections through the outer region of the pericarps of three Louisiana Capsicums. × 300. *L*, Capsicum, La. Long; *S*, Capsicum, La. Sport; *T*, Tabasco. *ep*, epidermis, *h*, hypodermis; *m*, mesocarp.

plastids and oil droplets and elaioplastids, fragments containing groups of yellow stone cells of the endocarp, the latter with sinuate, porous and beaded vertical walls up to 15μ in thickness; fragments of the epidermis of the seed coat with large, sinuate, porous stone cells with thick, lignified walls, the latter frequently up to 38μ in thickness, occasionally up to 64μ in thickness; fragments of thin-walled cells of endocarp with cellulose walls and containing orange to red or brown chromoplastids and oil globules, often adherent to stone cells; numerous fragments of epicarp with beaded, polygonal to irregularly quadrangular or triangular vertical walls up to 11.4μ in thickness; fragments of the endosperm showing small-celled parenchyma containing aleurone grains and fixed oil globules.

Moisture.—One sample of authentic ground drug was examined for moisture determination according to the U. S. P. method and found to contain 9.77%.

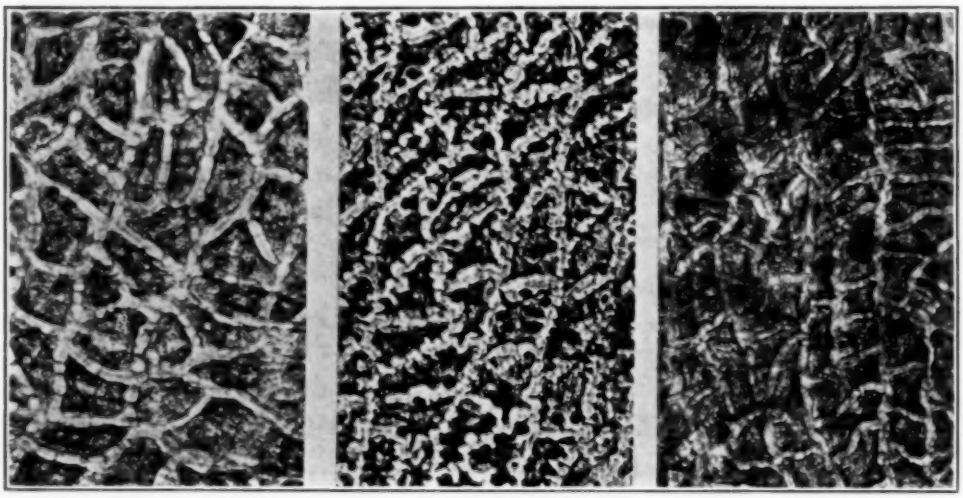
Ash.—The total ash of one authentic sample was 4.95% and the acid-insoluble ash of this sample was 0.12%. The total ash of 10 other samples claimed to be

authentic and reported by J. Harney varied from 4.20% to 5.50% while the acid-insoluble ash of these varied from 0.10% to 0.35%.

Ether Extract.—The ether extract, as determined by the U. S. P. method for one authenticated sample was 16.4%, the volatile extractive of this being 1.63% and the non-volatile extract, 14.85%. The non-volatile ether extract of 10 samples reported upon by J. Harney varied from 15.25% to 17.40%.

CAPSICUM, LOUISIANA SPORT.

The plants received from Louisiana were compact-bushy, up to $2^1/_2$ ft. in height with petiolate, ovate, acuminate leaves. The fruits were oblong-conical, red, glossy, up to 5.5 cm. in length and up to 13 mm. in diameter, and borne on ends of peduncles that attained the length of 2.5 cm. (See Figs. 2 and 4*B*.)



L *S* *T*

Fig. 6.—Surface sections of the epicarps of three Louisiana grown Capsicums. × 200. *L*, La. Long; *S*, La. Sport; *T*, Tabasco.

According to information received from Professor Julian C. Miller of Louisiana State University, the old original Sport Capsicum was probably introduced into Louisiana around 1900 by R. E. Thompson, Sr., of Norwood, La., and is stated by R. E. Thompson, Jr., to be of Oriental origin, the seed coming from Japan. The new Louisiana Sport which has been developed by Professor J. C. Miller is darker and more prolific and represents a hybrid between the old Louisiana Sport and the Japanese variety of Capsicum known as "Honka."

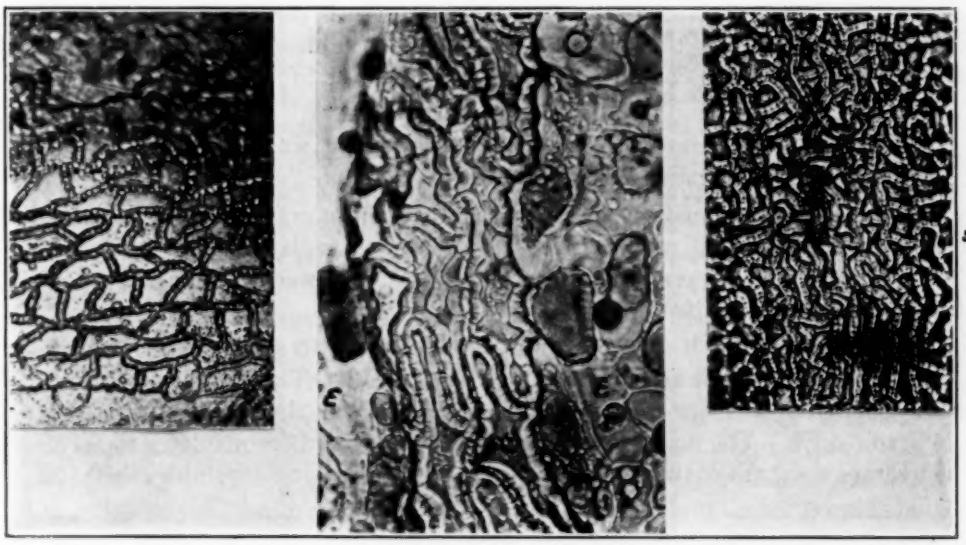
Description of Fruits.—Dried fruits oblong-conical, red to reddish brown, glossy, up to 5.5 cm. long and up to 13 mm. in diameter, some with a saucer-shaped, gamopetalous calyx having 5 reduced, blunt teeth; odor aromatic and sternutatory, upon crushing; taste of pericarp and seeds very pungent.

Histology.—(A) Pericarp. Transverse sections of the pericarp showed (1) an epicarp of epidermal cells up to 38μ deep and from 34μ to 76μ in length with cuticularized outer, inner and radial walls, the outer walls with cuticle up to 26.6μ in

thickness; (2) a mesocarp consisting of an outer hypodermis of from one, two or rarely three rows of hypodermal cells with cuticularized walls, a broad middle zone of parenchyma whose cells contain red, orange and yellow chromoplastids and fixed oil droplets, which is traversed by bundles, and an inner zone of one layer of giant cells; (3) an endocarp of a single row of stone cells interspersed with thin-walled inner epidermal cells. (See Figs. 5, 6 and 7*S*.)

Surface sections of the epicarp showed the cells to be quadrangular, rectangular, polygonal and triangular in shape with a striated cuticle. The vertical walls of the epicarp cells were yellow and beaded. The cells were 34μ to 76μ in length and 20μ to 64μ in width.

Surface sections of the hypodermis showed the cells to be of rounded to irregu-



L *S* *T*

Fig. 7.—Surface sections of portions of the endocarp of three Louisiana Capsicums. × 80. *L*, Capsicum, La. Long; *S*, Capsicum, La. Sport; *T*, Tabasco. *E*, soft, inner epidermal cells of endocarp; *st*, stone cells of endocarp.

larly rounded outline with colorless, beaded, cuticularized walls and thickened angles and containing red and orange chromoplastids and oil globules.

Surface sections of the endocarp showed irregular groups of sinuate stone cells separated by thin-walled, inner epidermal cells. The stone cells possessed sinuate, lignified and beaded vertical walls from 3.8μ to 15.2μ in thickness. The endocarp stone cells contained yellow to orange-colored chromoplastids.

(B) Seed. Transverse sections of the seed showed similar regions to those of the other Capsicums. The outer epidermis of the seed coat possessed extremely lignified stone cells, the depth of the larger stone cells being up to 156μ. In surface sections these stone cells had sinuous, contorted, vertical walls up to 26.6μ in thickness. The cells were up to 342μ in length, the walls being usually narrower than the lumen.

The endosperm and embryo contained small-celled parenchyma with aleurone and fixed oil contents. No crystals were observed in the endosperm.

Powdered Louisiana Sport Capsicum.—Red. Under the microscope it showed numerous fragments of epicarp composed of quadrangular, rectangular, polygonal and triangular cells with cuticularized walls, the cells being from 34μ to 76μ in length, 20μ to 64μ in width and up to 38μ in depth, occasional rows of cells in some fragments being in parallel series as in African Chillies; fragments of hypodermis with rounded to irregularly rounded cells with colorless, beaded, cuticularized walls and thickened angles and containing red or orange, irregular shaped chromoplastids and oil globules; fragments of endocarp with irregularly sinuate, beaded stone cells containing chromoplastids, the walls of which are up to 11.4μ in thickness with adherent thin-walled parenchyma containing red and yellow chromoplastids and orange oil globules; numerous yellow, irregular fragments of the epidermis of the seed coat composed of irregular, strongly lignified stone cells with very irregular lumen, the walls being frequently thicker than the lumen; numerous fragments of the endosperm and embryo consisting of parenchyma containing aleurone grains and fixed oil globules.

Moisture.—One sample of authentic ground drug was determined by the U. S. P. method to contain 8.78% of moisture.

Ether Extract.—The total ether extract of a recently ground sample of authenticated fruit was 18.395 of which 0.64% represented volatile ether extract and 17.75% represented non-volatile ether extract. The non-volatile ether extract of 12 other samples varied from 17.02% to 20.45%.

Ash.—The total ash of a recently ground authentic specimen of fruit was 5.38%, the acid-insoluble ash of this sample being 0.11%. The total ash determined on 12 other samples from different crops grown at New Iberia, La., varied from 3.75% to 5.40%. The acid-insoluble ash of these varied from 0.10% to 0.25%. The average total ash of these was 4.52% and the average acid-insoluble ash, 0.15%.

TABASCO PEPPER.

The Tabasco plants were identified as *Capsicum annuum* L. **var.** *conoides* Irish. This variety of Red Pepper was probably introduced into Louisiana from the state of Tabasco in Mexico and has been grown on a large scale by the McIlhenny family for several generations on Avery Island, La. The fruit has been chiefly employed in the preparation of Tabasco sauce. It was introduced in 1840.

The plants examined were suffrutescent with ovate leaves from 1 to 3 in. long and from $^3/_4$ to 2 in. in width. The flowers were small, greenish white and borne on slender, erect peduncles up to 3.3 cm. in length. The calyx was obconical or cup-shaped, embracing the base of the fruit, the corolla greenish white, gamopetalous. The fruits were very pungent and represent sub-conical to oblong-conical berries, from 2 to 4 cm. in length and up to 9 mm. in thickness. The plants answered to the description by Irish (1). (See Figs. 3 and 4*D*.)

J. C. Miller (4) recently reported having developed two strains of the Tabasco pepper, one, bearing a long slender fruit intended for pickling whole, and the second, bearing a shorter fruit which dehisced from the bush very readily in the green state. The latter type is used in making sauce, since its pericarp is thicker.

Description of Fruit.—The dried fruits were sub-conical to conical-oblong with a tubular-campanulate (cup-shaped) calyx embracing the base of the fruit. The peduncles, present on some of the fruits were slender and varied from 28 mm. to 33 mm. in length. The fruits were from 2 to 4 cm. in length and up to 9 mm. in thickness, red to salmon red, sometimes blotched with yellow, the wall of the pericarp being up to 1 mm. in thickness. The wall of the pericarp in preserved fruits was up to 2 mm. at the base. The seeds were sub-orbicular, albuminous, thickened along margin, with a prominent beak at the micropyle and up to 3 mm. in diameter.

Histology.—(A) Pericarp. Under the microscope, transverse sections of the pericarp presented for examination (1) an epicarp of tangentially elongated epidermal cells with highly cuticularized outer and radial walls, the length of these cells being from 19μ to 76μ and their depth up to 30.4μ. The thickness of the outer cuticularized wall was frequently up to 19μ. (2) The mesocarp consisted of an outer region of 3 to 4 layers of tangentially elongated, collenchyma cells containing red, orange and yellow chromoplastids and oil globules, the cells becoming larger inwardly, a broad middle zone of large-celled parenchyma with chromoplastid and oil contents, some of the cells containing in addition monoclinic prisms. This zone was traversed by bundles. Bounding the inner margin of the middle zone was a layer of large giant cells separated by triangular strands of thin-walled, small-celled parenchyma. (3) The endocarp consisted of a layer of stone cells beneath each giant cell separated by thin-walled inner epidermal cells between adjacent stone cell layers. The stone cells possessed beaded, lignified, outer, radial and inner walls and were somewhat square in shape. In some sections the stone cells were continuous beneath the parenchyma separating the lower portions of the giant cells. (See Figs. 5, 6 and 7*T*.)

(B) Seed. Transverse sections of the seed showed: (1) an outer epidermis of the seed coat with large, yellow stone cells with greatly thickened, lignified, radial and inner walls, the cells being larger along the thickened margin of the seed where they were up to 198μ in radial length; (2) an arrow zone of collapsed parenchyma, thicker along the margin of the seed; (3) an inner epidermis of the seed coat of tangentially elongated, more or less collapsed cells; (4) a perisperm consisting of a layer of square to tangentially elongated cells with aleurone contents; (5) an endosperm of varying diameter composed of moderately thick-walled parenchyma containing tiny protein granules and oil globules. A number of monoclinic prisms were observed in the cells of this region. The outermost layer of cells of the endosperm possessed greatly thickened walls. (6) An embryo of small-celled parenchyma and epidermis.

Surface sections of the epicarp showed mostly irregularly rectangular or quadrangular, occasionally irregularly polygonal or triangular epidermal cells, from 30.4μ to 76μ in length and 13.3μ to 19μ in width frequently arranged in parallel rows.

Surface sections of the seed coat showed the outer epidermal cells to be sinuous, contorted with irregularly thickened, lignified, vertical walls, up to 202μ in length, the width of the walls up to 26.6μ.

Powdered Tabasco.—Reddish brown. Numerous fragments of large-celled parenchyma of the mesocarp containing red, orange and yellow chromoplastids and yellow oil globules and small elaioplastids; numerous pale yellow oil globules; fragments of endocarp with irregular, sinuate stone cells, the vertical walls of which

are up to about 7.5μ in thickness adherent to which are frequently thin-walled inner epidermal cells with irregularly shaped yellow chromoplastids and oil globules; fragments of epicarp composed of polygonal, quadrangular, rectangular or irregular cells with beaded, yellow, vertical cuticularized walls, the latter up to 7.6μ in thickness, many of the cells often in parallel series; fragments of the epidermis of seed coat with much contorted, sinuate, lignified stone cells with irregularly thickened walls containing many broad pore canals; fragments of small-celled parenchyma of the endosperm containing tiny aleurone grains, fixed oil globules and occasional monoclinic prisms.

Moisture.—One recently ground authentic sample of Tabasco was found to contain 7.6% of moisture.

Ether Extract.—The ether extract of one recently ground authentic sample was found to be 20.93% of which 0.92% was volatile and 20.01% was non-volatile. The non-volatile ether extract of 10 samples of Tabasco obtained from different crops ran from 17.25% to 20.25% with an average of 18.1%.

Ash.—The total ash of one recently obtained sample of authentic ground Tabasco was 4.57% and the acid-insoluble ash, 0.08%. The total ash on 10 samples of ground Tabasco obtained from different crops ran from 3.5% to 5.1% with an average of 4.1%. The acid-insoluble ash of these ran from 0.08% to 0.10% with an average of 0.94%.

PUNGENCY TESTS.

The U. S. P. XI pungency test was carried out with the three varieties of Louisiana Capsicum and a control which represented recently ground African Capsicum received from S. B. Penick & Co. on a series of three individuals with the following results:

La. Longs	Positive 0	Negative 3
La. Sports	Positive 1	Negative 2
Tabasco	Positive 2	Negative 1
African Capsicum	Positive 2	Negative 1

A second series of tests was run on 25 individuals, using the same preparation employed in the U. S. P. pungency test, with the following results.

La. Longs	Positive 0	Negative 25
La. Sports	Positive 8	Negative 17
Tabasco	Positive 16	Negative 9
African Capsicum	Positive 19	Negative 6

It is apparent from the results of the first series of U. S. P. tests that the samples of African and Tabasco peppers met the pungency requirement, 2 out of 3 individuals responding positively.

In the second series of tests in which 25 persons were used, the U. S. P. African Capsicum alone met the official requirement with Tabasco coming within a fraction of an individual from meeting it.

If, however, the group of 25 individuals were to be divided into groups of 3 consecutive persons and the results analyzed, it was found that in 2 groups to which the preparation of African Capsicum had been administered only 1 out of 3 individuals met the pungency test, whereas in one group to which the preparation of La. Sport Capsicum had been administered all three responded positively to the test.

The variability of sensitivity of humans to the Capsicum pungency test is 50:1, according to Crosbie and Munch (5), who found it necessary to standardize the test animal against piperine or capsaicin.

It is, accordingly, evident that owing to the great variability of sensitivity of individuals to the present U. S. P. pungency test, this test is not reliable as a means for evaluating Capsicum.

When powdered Tabasco and La. Sport Capsicum were tasted by the tip of the tongue by 12 non-standardized individuals they appeared as pungent as powdered African Capsicum.

It would seem urgent that either the U. S. P. method be revised by first standardizing humans or that a chemical test probably based on the capsaicin content be devised as a standard of assay for this drug.

REFERENCES.

(1) Irish, H. C., "A Revision of the Genus Capsicum with Especial Reference to Garden Varieties," 9th Ann. Rept., Missouri Bot. Gard., 1898, 53.

(2) Martius, C. F. P., *Fl. Braz.*, 10, 147 (1846).

(3) Bailey, L. H., *Gentes Herbarum*, 1, 128–129 (1923).

(4) Miller, J. C., Rept. La. St. Exp. Sta. (1937).

(5) Munch, J. C., and Crosbie, H., "Bioassays of Capsicum and Chillies," JOUR. A. PH. A., 18 (1929), 1236–1246.

THE EFFECT OF PEPTONE ON THE RESISTANCE OF STAPHYLOCOCCUS AUREUS.*

BY GEORGE F. REDDISH[1] AND ELLA M. BURLINGAME.

It is a well-known fact that the different brands of commercial peptone vary as to their chemical composition. Different batches of the same brand of peptone will also vary chemically, dependent, probably, on the degree of digestion. We have some evidence to the effect that there is a correlation between the state of digestion and the nutritive value of peptone, but exactly what chemical factors are responsible for these differences is not known at this time.

The *growth-promoting* value of the different peptones is not the only factor to be considered. Different peptones may give equally luxuriant growth of certain bacteria and yet the condition of these organisms will vary considerably. In making diphtheria toxin, tetanus toxin, etc., certain peptones will give good growth of the organisms in broth, but it is usually found that one certain peptone will give toxin of a higher potency than the others. For this reason, we cannot be guided entirely by the growth-promoting property of peptones in choosing the brand to be used in bacteriological work. For plate counting in milk and water examination, however, the peptone chosen must possess maximum growth-promoting properties and give the maximum number of colonies. The condition of the organisms after they have grown on the plates is of no importance so long as the colonies are large enough to be easily counted.

* Presented before Section N, Sub-Section on Pharmacy, at the meeting of the American Association for the Advancement of Science, December 27, 1937.

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In testing disinfectants and antiseptics, however, the *condition* of the test organisms, their vigor and resistance is of paramount importance. The peptone used in the media in this work should give good growth, of course, but the media must be such that the resistance of these bacteria will be retained and conserved. The vigor of the test organisms must be maintained at a level equal to their resistance when freshly isolated.

It is for this reason that so much emphasis is placed on the character of the media used in the bacteriological testing of disinfectants and antiseptics. Comparative tests using different peptones have been made during recent years and the specific brand of peptone for use in this work is now specified. In the original Hygienic Laboratory Method for disinfectant standardization (1) published in 1912, however, the peptone was not specified. It was simply stated that the broth to be used should be "in exact accordance with the standard methods adopted by the American Public Health Association for water analysis." It was soon recognized that the peptone found suitable for use in water analysis would not necessarily be applicable for use in broth for disinfectant testing. Consequently, in the 1921 revision of the Hygienic Laboratory Method (2), this error was corrected and a peptone suitable for disinfectant testing was specified. The peptone specified is that made by Armour and Company.

This peptone has been found satisfactory for sixteen years and is still recognized as being better suited for work of this kind than other brands on the market. In the methods of testing disinfectants and antiseptics published by Reddish (3), (4), Armour's peptone is specified for the broth and agar to be used in these tests. In spite of the fact that this peptone is specified in the American standard methods for testing antiseptics and disinfectants, many laboratories throughout the country have ignored this important specification. The result is that widely different results have been obtained by these laboratories. Some of these laboratories have reported results by standard methods of test and in giving the details have even stated that a peptone was used which is different from that specified in these methods. To make matters worse, the substituted peptone often is one which actually weakens the test organisms so that the results obtained indicate that the products tested are much more germicidal than they really are. Tests in my own laboratory have shown that one such peptone will render *Staphylococcus aureus* quite weak within 48 hours, that is, when transferred twice at 24-hour intervals in broth made with this particular brand of peptone. Such a weakened culture is obviously not fit for use as a test organism. *Staphylococcus aureus* is the standard test organism used in testing antiseptics and is employed by the U. S. Food and Drug Administration in their control work on disinfectants and antiseptics (5). The normal resistance of this organism has been thoroughly studied by Reddish (6) and a phenol standard for it has been established.

In order to demonstrate again the effect of different commercial brands of peptone on the resistance of this organism, ten brands of peptone were used in the present study.[1] The following brands were employed: Wilson, Witte, Merck, Stearns, Parke, Davis and Company, Fairchild, Bacto, Bacto-Proteose, Bacto-Tryptophane, and Armour. Broth of the following composition was made from each of these peptones: 1% peptone, 0.5% beef extract and 0.5% NaCl, dis-

[1] Part of a study conducted in coöperation with Emil G. Klarmann, Lehn and Fink, Inc., Bloomfield, N. J., and Burton G. Philbrick, Skinner and Sherman, Inc., Boston, Mass.

solved in water and adjusted to p_H 6.8. These ten broths were inoculated with *Staphylococcus aureus* from an agar slant culture and transfers made from each broth culture at intervals of 24 hours and incubated at 37° C. At the end of the third, seventh and tenth day, these ten cultures of *Staphylococcus aureus* were tested for resistance against phenol and an antiseptic similar to Liquor Antisepticus.

Staphylococcus aureus by standard F. D. A. test (using Armour's Peptone) is not killed by 1–60 phenol in 5 minutes nor by 1–70 phenol in 15 minutes at 20° C. and by 1–80 phenol in 5 minutes and 1–90 in 10 minutes at 37° C. The time periods, 5, 10 and 15 minutes, are rather broad for detecting small differences in resistance of these cultures. The average results from four sets of such tests indicate that these ten cultures (*Staphylococcus aureus* grown in broth made with ten different brands of peptone) are of approximately equal resistance. While there was a difference in the character of the culture, apparently this would not affect materially the resistance to phenol as determined in 5-, 10- and 15-minute time periods. The results obtained with each peptone on the third, seventh and tenth days were often approximately the same as that given by the Armour's peptone culture. However, the growth and resistance of the Armour's peptone culture was always uniform, whereas some of the other cultures were granular and clumpy and varied in resistance. Five of these ten cultures gave growth in broth which was very granular with large clumps, whereas the other five gave a more uniform growth with only slight clumping. While this is a factor in obtaining uniform results in short time periods, there was not always sufficient difference in the cultures to show a marked difference in resistance in the 5-, 10- and 15-minute time periods.

Since the time periods used in the phenol tests were 5, 10 and 15 minutes, the differences in resistance of these ten cultures were not so accurately demonstrated. In order to bring out differences in resistance it was necessary to prepare a special antiseptic which would not kill the Armour peptone broth culture in 2 minutes, but would kill in 3 minutes by F. D. A. test at 37° C. When the resistance of the other cultures was lowered, they were killed in time periods ranging from 30 seconds to 2 minutes. Tests with this antiseptic were found to be more accurate and show differences in resistance of these cultures which were not revealed with phenol at 5-, 10- and 15-minute time periods. In this report this solution will be designated as Antiseptic "A."

TABLE I.—F. D. A. METHOD, STRAPHYLOCOCCUS AUREUS—0.5 CC. OF BROTH CULTURE TO 5.0 CC. OF ANTISEPTIC "A" AT 37° C.

	3rd Day.				7th Day.				10th Day.			
Brand of Peptone.	30".	1'.	2'.	3'.	30".	1'.	2'.	3'.	30".	1'.	2'.	3'.
Wilson	+	+	0	0	+	+	0	0	+	+	0	0
Witte	+	+	0	0	+	+	0	0	+	+	0	0
Merck	0	0	0	0	0	0	0	0	+	0	0	0
Stearns	+	+	0	0	+	+	0	0	+	+	0	0
Parke, Davis & Co.	+	+	0	0	+	0	0	0	+	0	0	0
Fairchild	+	0	0	0	+	0	0	0	+	0	0	0
Bacto	+	0	0	0	+	0	0	0	+	0	0	0
Bacto-Proteose	+	+	0	0	+	+	0	0	+	+	0	0
Bacto-Tryptophane	+	+	0	0	+	+	0	0	+	+	0	0
Armour	+	+	+	0	+	+	+	0	+	+	+	0

When Antiseptic "A" was used at time periods of 30 seconds, 1, 2 and 3 minutes, it was possible to show differences in resistance between these ten cultures. Considering Armour's peptone as a standard for comparison, since this is the one specified in the American standard methods for testing antiseptics and disinfectants, we found that the resistance of *Staphylococcus*

aureus was reduced by the other peptones used. Four of these peptones were found to have a very definite weakening effect on *Staphylococcus aureus*, reducing its resistance so that it was killed within 1 minute, and in one case 30 seconds, whereas the culture grown in Armour's peptone was not killed within 2 minutes. The results of these tests are given in Table I.

It is shown in Table I that whereas the culture of *Staphylococcus aureus* grown in broth made with Armour's peptone was not killed by Antiseptic "A" within 2 minutes, the cultures in broth made from the other peptones were killed within 2 minutes and four of them were killed within 1 minute. While these differences do not seem great, it is shown that Armour's peptone broth is best suited for retaining the resistance of this test organism. The very fact that a peptone will weaken a test organism at all, regardless of how much, is sufficient reason for excluding its use in media employed for this purpose. Since Armour's peptone assures uniform cultures of *Staphylococcus aureus* in broth and will maintain normal resistance of this test organism, this peptone only should be employed in the testing of disinfectants and antiseptics for germicidal activity against this standard test organism.

SUMMARY.

It is shown in the present study that Armour's peptone is best suited for use in media employed for growing *Staphylococcus aureus* for use in testing antiseptics and disinfectants. The resistance of this standard test organism is maintained consistently and uniformly when broth made with this peptone is used, whereas when other peptones are employed the resistance of this organism is reduced to a significant degree. For this reason Armour's peptone should continue to be specified for use in media employed in the testing of antiseptics and disinfectants for germicidal activity.

REFERENCES.

(1) Hygienic Laboratory Bulletin No. 82, April 1912.

(2) Public Health Reports (Reprint 675), 36, 1559 (1921).

(3) Reddish, George F., "Examination of Disinfectants," *Am. J. Pub. Health*, 17, 320–329 (1927).

(4) Reddish, George F., "Methods of Testing Antiseptics," *J. Lab. Clin. Med.*, 14, 7, 649–658 (April 1929).

(5) U. S. Dept. of Agriculture, Circular 198 (1931).

(6) Reddish, George F., "The Resistance to Phenol of *Staphylococcus aureus*," *Am. J. Pub. Health*, 15, 534–538 (1925).

COURSE IN PUBLIC HEALTH FOR PHARMACISTS.

A tentative course in Pharmacy has been prepared for the Pharmaceutical Syllabus. It includes Infections, Non-Infections, Nutrition, Hygiene of the Digestive System; Social Hygiene; the Eye and Observation of Vision; the Ear and Observation of Hearing; the Musco-Skeletal System; Cardio-Vascular-Renal System; Accident, First Aid, covering the subjects quite thoroughly.

The sub-committee on Public Health have charge: Haven Emmerson, Robert P. Fischelis, Albert Hardy, B. E. Holsendorf, P.A.P., Rufus A. Lyman, Carl F. Meyer, Earl B. Phelps, M. J. Rosenam, Leonard J. Picoli, *chairman*.

HOSPITAL PHARMACY'S OPPORTUNITY.*

W. WILSON MCNEARY.[1]

I am pleased to have the opportunity to present some observations on the opportunities for self-preservation and development of the profession of Pharmacy through the medium of the hospital. Notwithstanding the cry that pharmacy is a decaying profession, I make the assertion that when the hospital pharmacy closes its office or dispensary the hospital closes its doors. In other words a modern hospital cannot exist without a modern pharmacy. (There are some 7000 hospitals in the U. S. to-day.) However, when I say a modern pharmacy, I do not mean the so-called modern corner drug store because the function of one and that of the other are as far apart almost as the poles. One is almost strictly commercial and the other entirely professional.

Whether we like it or not there has been a decided trend toward hospitalization, particularly during the last few decades, and patients who, twenty years ago, would have been treated at home now go to hospitals. Only those associated with hospitals fully realize this and with voluntary group hospitalization plans developing all over the country the tendency is going to increase.

Unfortunately up to the present time there has been little or no recognition of hospital pharmacists by accrediting organizations or supervision or standardization by state boards of hospital pharmacies. The only genuine interest taken in the hospital pharmacy has been by the administrator of the hospital, and, if his standards are high in other respects he is likely to employ a well-qualified pharmacist and the rest follows. If he is, as too many are, interested in costs more than in service, the pharmacy is bound to suffer.

How has it suffered? It has suffered because the hospital pharmacist is not sufficiently qualified for his work. Now here is the rub. A good hospital pharmacist should be first, well educated basically, fit to do more than just compound the stock prescriptions. He should have intelligence of a high character, also a high personality quotient, the ability to discourse intelligently not only on pharmaceutical matters but on medical subjects as well. He should be able to direct the sterilization procedures of the Operating Rooms. He should be qualified to be the sanitary officer or inspector of the institution. In fact he should be the general and specific knowledge man of the institution, one who can be consulted, not only by the medical staff but by the administrator and other personnel of the hospital.

Now what I regard as one of the most important functions of the hospital pharmacist is the opportunity, backed by ability to teach the new internes prescription writing and sufficient knowledge of pharmacy that they may be able to order intelligently what they want from the vast storehouse of our modern materia medica.

We all know that pharmacy is not taught in most of the medical schools, so why should we blame the modern physician for not doing something, the knowledge of which has been denied him? I see little possibility of having pharmacy taught in medical schools. There are too many other basic subjects already, but why not teach them this subject during their interneship? And who is there, other than the

* Presented before Sub-Section on Hospital Pharmacy, New York meeting, 1937.

[1] Director, American Hospital for Diseases of the Stomach, Philadelphia, Pa.

hospital pharmacist, who should be properly qualified to teach this branch of medicine to them?

I will go further and say that an effort should be made to have the hospital pharmacy included in the rotating services of the hospital. If this could be accomplished the new generation of doctors would be greatly helped. They would learn to eschew the semi-proprietary polypharmaceutical manufactures' salesmen, write U. S. P. and N. F. preparations and only use those newer remedies, the products of real scientific research, which have proven valuable to the profession.

A TRANSPARENT EMULSION OF OIL OF TURPENTINE.*

BY P. A. FOOTE[1] AND C. H. GILLILAND.

Pharmaceutical interest in emulsions seems to never wane. It is truly one of the fine arts of the apothecary to make a good stable emulsion which is therapeutically efficient, palatable and pleasing to the eye. To those who claim that there is no such a thing as pharmaceutical research let them enter this field and they will soon change their mind. Why does this interest continue? There are various reasons, a discussion of which has no place in this paper; however, the authors wonder if one reason might not be the fact that they are more or less spectacular and it is human nature to be interested in spectacular things. Indeed, a successful pharmacist recently advised us that his interest in pharmacy began at the age of five when he witnessed the making of an emulsion. To him it was magic because a dark liquid (compound solution of cresol) was added to clear water and the result was a milk-like preparation. It would not have been magic to the boy if oil of turpentine and water had been mixed in such a way as to give a transparent preparation. Neither would it be magic to the young pharmacy student who has just been initiated into emulsion technique, but he would no doubt be surprised.

Transparent emulsions are made by equalizing the refractive indices of both phases at the same temperature. The subject is not new but it deserves more attention. Some pharmacy textbooks briefly devote a few lines to the theory of them but give no working examples. Other texts do not mention them. The result is that many pharmacy students graduate without having heard of such preparations. Probably the majority of pharmacists have never seen one. The report on transparent emulsions by Whitmore and Linehan (1) gave the authors further interest in the subject with the result that the task of making a transparent emulsion of oil of turpentine of U. S. P. strength was assigned to the junior author as an "Honors" problem for graduation. It is herewith presented hoping that it will arouse more interest in this subject.

PROCEDURE.

All determinations were made with an Abbé refractometer at 23° C.

1. Gelatin Solution.—One gram of high-grade gelatin is dissolved in 10 cc. of hot distilled water, n_d 1.3500.

2. Glycero-Gelatin Solution.—Add to No. 1 an equal volume of U. S. P. glycerin. Product, n_d 1.4171.

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* Section on Practical Pharmacy and Dispensing, A. PH. A., New York meeting, 1937.

[1] Professor of Pharmacy, University of Florida.

3. Invert Sugar Solution.—Dissolve 2.5 Gm. of tartaric acid in 100 cc. of distilled water, then 200 Gm. of sucrose and heat at 100° C. for two and one-half hours, n_d 1.4963. After twelve hours n_d 1.4838. After two weeks n_d 1.4843. If caramelized decolorize with activated charcoal.

4. Combine by Weight 10 Parts of No. 2 with 100 Parts of No. 3.—This will probably have an idex of refraction slightly higher than the oil of turpentine n_d 1.4701. Water is then cautiously incorporated to reduce the index of refraction to that of the oil. This may require as much as 10% of water.

5. Emulsification.—Place about 10 cc. of No. 4 in a mortar and emulsify a few drops of the oil. Alternately add increasing amounts of each until 15 cc. of the oil has been incorporated and the volume of the finished product is 100 cc. For finer dispersion of the oil, which gives greater stability, pass the emulsion through a hand homogenizer two or three times. Bottle and invert to allow the air and foam to rise. When clear pour into another bottle. It is of course an oil-in-water type.

DISCUSSION.

Because there is a wide difference between the index of refraction of water (1.3328) and the oils, the problem of making transparent emulsions is largely one of finding physiologically inert substances to either build up the refractive index of the aqueous phase or to lower that of the oil phase. The former appears to be easier. Solutions of invert sugar, honey, glucose and Karo corn syrup can be used. The authors found it convenient to prepare invert sugar solutions by heating with a small amount of tartaric acid. Other acids might be used as catalysts but it is our opinion that tartaric acid improves the flavor of this particular emulsion. If necessary the index of refraction of this solution can be conveniently raised by adding liquid glucose (n_d 1.5023). If the emulsion is not perfectly transparent at the adjusted temperature, the index of refraction of the primary phase may be lowered or increased by adding small amounts of water or liquid glucose. To find out which is needed take the index of refraction of the emulsion. If this is higher than the oil, add water. If it is lower, add liquid glucose.

This emulsion appears to be very stable for at least a year when standing in diffused light at room temperature. After eighteen months a few crystals were deposited. After two years it became quite yellow which is to be expected of the turpentine and the sugar in the presence of an acid. A centrifuge at 1800 r. p. m. will readily break the emulsion in a few minutes if prepared by the mortar method alone. Similar treatment will not break it if it has been put through a homogenizer.

There is a peculiar fascination about this subject which has led us to make other transparent emulsions for a later report. The newer emulsifying agents and other chemicals now available in commercial quantities offer interesting possibilities.

SUMMARY.

1. The subject of transparent emulsions deserves more attention.

2. A procedure is given for making a transparent emulsion of oil of turpentine.

REFERENCE.

(1) Whitmore, W. F., and Linehan, R. E., *Ind. Eng. Chem.*, 21, 878 (1929).

THE EARLIEST HOSPITALS.*

BY ELEANOR KAIRIS.[1]

The modern hospital is the result of a gradual evolution from institutions which had their nascence in antiquity. The temples of Egypt and Greece, the surgeries, the valetudinaria, and the Roman military hospitals, all helped to pave the way for the modern establishments which followed. Because of their pagan implications, these early institutions were closed in 335 A. D. by a decree of Constantine. Some were completely abolished while others only ceased to function. So great a need had been created for these establishments, however, that those not completely destroyed were obliged to re-open under new influence and supervision.

The earliest institutional care of patients had its inception in the ancient Egyptian and Greek temples. In most instances, these temples were dedicated to gods of healing, or as is generally believed now, to rational beings whose mundane achievements earned them deification. Religious and philanthropic in character, they were equipped and manned to assuage both the flesh and the spirit.

In the beginning, cures in the temples were effected by subordinating rational methods to mystic ritual. These outward manifestations of mysticism, magic and cant, were resorted to, according to Gauthier, in order "to gain ascendency over the populace." It is said that Pythagoras, who exercised the earliest and most lasting influence on medicine, learned from the Egyptian priests how to influence his patients through magical charms and incantations. He felt that to eliminate certain mystical rites, which were as much a part of the patient as the pain which brought him, would result in a loss of confidence. Hence he allowed it to be supposed that the magic formula was the important part of the cure. Breasted, in his introduction to the *Edwin Smith Surgical Papyrus*, said that certain traditional practices in medical treatment, which were wholly or chiefly magical, never disappeared. These views, implicitly followed by the common people, died hard. When Pythagoras founded his great Brotherhood he had two types of disciples: those who "had been proven," and "those who remained to be proven." There were secret doctrines for those who "had been proven," precepts teaching a combination of science and magic, supplementing one with the other. When the Order was dissolved in the second half of the 5th century B. C. a disagreement as to doctrine caused a rift in the ranks of the Brotherhood. One group of disciples cast off the air of mystery and acknowledged that they cured only by natural means. The other group, however, engaged in even more mysticism, repeating glibly the philosophical catchwords of their school, and concocted a psuedo-scientific system which dispensed with all proof.

Magic and mysticism in the temples started with the oracles who were first consulted for any purpose, and eventually for health. When the oracles were overwhelmed with consultants they called in the priests, who with their practical knowledge of simple remedies, proved able allies. When the requests became even more numerous, one priest devoted all his time to the observance of ritual while a colleague devoted himself to cures. The chief physicians to the Pharaohs were high ecclesiastics and their titles, still extant on many of the inscribed stelæ, indicate

* Presented before Sub-Section on Hospital Pharmacy, New York meeting, 1937.

[1] Pharmacist, Sinai Hospital, Baltimore, Md.

that they were the heads of staffs of physicians attached to the court and the temples.

Nothing was spared to make the temples imposing and inviting. They were situated geographically in supremely attractive scenery. Ivory doors inlaid with gold, decorative sculptures, majestic statuary—all had a tendency to impress the patient. And yet, it was not only the æsthetic side which was nurtured. Fresh air, sunshine, a good water supply, freedom from external disturbances were combined factors which decided the site of a temple of healing.

Procedure in the temple followed a very definite form. On arriving, the patient was conducted through preliminary stages of ritualistic bathing and dieting. After these preliminaries he was led to a life-sized statue of the god to whom he offered prayers and oblations. Then the priest-physician conducted the patient through the temple, stimulating his imagination by showing him numerous votive offerings representing parts of the body which had been cured in others. These adorned the walls and columns of the temple. A pair of silver eyes, or a relief in marble of a leg, were manifestations of gratitude for recovery. The tour concluded with singing of hymns in adoration of the god and an observance of religious dances. This entire procedure was a necessary propædeutic to induce a state of mind which would lend itself to suggestion.

After the patient's imagination had been sufficiently stimulated, he was led to the abaton where he was put to bed. This was a lofty, airy, sleeping chamber, its southern side an open colonnade. The beds, which bore a marked resemblance to portable cots, were placed between the columns of the portico. According to inscriptions, it was during this temple-sleep, or incubation, that the priest, masquerading as the god, appeared to the patient, commented on his ailment, and suggested a method of cure. It is difficult to say whether these visitations were merely hallucinations in individuals whose imaginations had been excited, or whether they had been given a drug to induce dreams. Nevertheless, the priest-physician availed himself of this situation and prescribed a course of treatment.

Long before incubation became a rite in the temples, the sick in Egypt and Babylonia were laid in public squares and much frequented by-ways. Those passing by who had suffered from a like disease and had found a remedy contributed of their knowledge and experience. After incubation became more widely practiced friends of the sick frequently went to the temple to see whether the god might reveal a cure for their ailing friends. When Alexander required medical care several of his friends laid themselves in the temple of Serapis to learn from the god if it would be to his advantage to come into the temple. It is said that the voice of the god replied negatively.

Whether incubation was indigenous in all ancient countries, or whether the idea was borrowed or diffused, is a problem for cultural anthropology. While it had an extensive development in the religions of the Euphrates and Tigris Valleys, and although it was widely practiced in the temples of Aesculapius throughout Greece, it may be conjectured that its genesis was in Egypt.

There is abundant evidence that among the methods of cure in the temples, even in earliest times, were surgery, use of drugs, hypnotic treatment, and the so-called miracle cures. Drugs were employed in forms requiring special preparation for administration. According to Jayne: "the more practical therapeutics of the

temple made use of external applications of lotions, ointments and remedies from plants." There were assistants to the priest-physicians whose assignment was to collect plants, to separate them into their constituent parts, and to prepare the leaves, blossoms, roots and juices. Mariette, in his voluminous work describing the excavations in the Great Temple at Dendérah, told of one large hall having the word "Laboratory" written over the door while an adjoining chamber was specified as a place where the preparations of the Laboratory were stored. The oils, ointments and essences, which were prepared here, undoubtedly were used in religious ceremonies, but it can be inferred with some degree of certainty that when the priest-physician felt that prayers and incantations had to be supplemented by a plaster or a poultice, the task was delegated to the "Laboratory." The large number of remedies and prescriptions cited in the *Papyrus Ebers* points to an elaborate Egyptian pharmacopœia and a highly developed art of pharmacy. The preparation of pills, plasters, poultices and ointments, required as much pharmaceutical technique in the days of the Pharaohs as they do to-day.

In Greece, too, there were temples dedicated to gods of healing, or to those whose seemingly miraculous cures had enrolled them among the deities. Just as in Egypt temple-sleep was widely practiced and excavations have revealed numerous votive offerings and inscriptions describing the varied methods of cure.

The Surgery or Iatrium (also written Jatreion) was in the nature of a private hospital in a physician's establishment, and was fully equipped with consulting rooms, pharmacies, operating rooms, and all the instruments then available. In *Kranken-Anstalten*, Meyer-Steineg wrote that the arrangement of rooms in the Iatrium was such that the patient was given every conceivable hygienic advantage. Draughts and the heat of the sun were avoided although there was an abundance of air and light. Part of the Iatrium was utilized for compounding drugs, another section for preparing foods and diets. There were quarters for the nursing staff and the physician's assistants. The Iatrium provided not only for the active staff but there is much probability that it was also a public laboratory for the sale of medicines. Aristotle's father, a distinguished physician and author of medical works, owned such an Iatrium. We are told, that when Aristotle returned from the wars he was obliged to dispose of the surgical building, apparatus and medicines, which he had inherited.

The Valetudinaria were hospitals in Rome so thoroughly equipped and manned with so complete a staff that a venerable tradition was indicated. Many are of the opinion that these hospitals ministered only to slaves but ancient literary commentators, especially Celsus and Seneca, mentioned no such restriction. In fact Seneca, when he wrote to a contemporary, referred to these hospitals frequently. He said, "and let us discuss our common woe as if we lay together in the same valetudinarium," which would lead one to suppose that admissions were not limited to slaves.

At permanent Roman army posts excellent military hospitals were established. The oldest revealed by excavation thus far is that of Carnuntum where remains of two periods were unearthed; a simple valetudinarium of the first century A. D. and a later enlargement. The new design was built on the corridor system and had both a kitchen and a pharmacy. With the decline of the Empire the military hospital

vanished almost completely and over a thousand years elapsed before provision again was made for sick and wounded soldiers.

One of the first hospitals following the edict of Constantine was a Nosocomium founded in 380 by Fabiola, a Roman lady of renowned piety and a close friend of St. Jerome's. She provided nourishment and such medical care as might be needed to the destitute sick whom she found on the public highways. Another hospital was built by Sir Basil, eight or ten years earlier, outside the walls of Cæsarea in Cappodocia.

In 550 the Emperor Justinian built the hospital of St. John at Jerusalem which subsequently became the cradle of the warlike Knights of Rhodes and Malta. Their original function was to care for sick pilgrims and later to minister to wounded crusaders. The earliest Christian hospitals were in the homes of the bishops but when the resources of the church proved insufficient the canons were ordered to give a tenth of their revenues to maintain the sick poor. Charlemagne decreed that the institutions should always be near the cathedral in order that the clergy might visit the sick. The monasteries of the Early and Middle Ages served both as hospices for pilgrims and as hospitals for the care of the sick. In early days the word "hospital" was used to denote a permanent retreat for the poor, infirm or insane, as well as a regular institution for the temporary reception of those requiring medical care.

In summation, the modern hospital is an outgrowth of institutions which arose in pagan antiquity through the temples, the surgeries, the valetudinaria and the Roman military hospitals. Archæological evidence confirming literary tradition attests to the existence of these institutions as early as 3000 B. C. In the beginning cures were effected by subordinating the rational to the mystical, but it may be conjectured that these outward manifestations were resorted to only "to gain ascendency over the populace," that it was the concrete substance employed which actually effected the cure.

The edict of Constantine closed these early institutions in 335 and the first hospitals or nosocomia under the new order were those founded by Fabiola and Sir Basil. The monastic period followed when hospitals were ecclesiastical rather than medical; they were for care rather than for cure. There was practically no further progress until the beginning of the 16th century and then began a slow but steady development which culminated in our present system, a system which had its genesis in remote antiquity.

REFERENCES.

Allbutt, Sir Clifford, Greek Medicine in Rome, MacMillan & Co., 1927.
Aravintinos, Temples of Aesculapius.
Blackwell, Basil, Magic in Greek and Latin Literature.
Breasted, G. H., The Edwin Smith Surgical Papyrus, Chicago, 1930.
Bryan, Cyril P., *The Papyrus Ebers*, New York, 1931.
Buck, Albert H., The Growth of Medicine from Earliest Times to 1800.
Burdett, Sir Henry, Hospitals and Asylums of the World, London, 1893.
Caton, Richard, The Temples and Ritual of Aesculapius, London, 1902.
Daremberg, C., Etat de la Medecine entre Homere et Hippocrate.
Daremberg, C., Histoire des Sciences Medicales.
Dawson, Warren R., The Beginnings in Egypt and Assyria Clio Medica Series.
Farnell, Louis Richard, The Gult of the Greek States.

Gauthier, L. P. A., L'Exercise de la Medecine dans les Temples chez les Peuples de L'Antiquite, Lyon, 1844.
Grote, George, Aristotle, London, 1883.
Hurry, Jamieson B., Imhotep, Oxford Univ. Press, 1926.
Jayne, Walter Addison, The Healing Gods of Ancient Civilizations, Yale Univ. Press, 1925.
Mariette-Bey, Auguste, Dendérah, Paris, 1875.
Neuburger, Max, History of Medicine, London, 1910 (Playfair Translation).
Petrie, W. M. Flinders, Social Life in Ancient Egypt, New York, 1923.
Singer, Charles, Short History of Medicine, Oxford, 1928.
Smith, G. Elliot, The Ancient Egyptians.
Steineg-Meyer, Kranken-Anstalten.
Stubbs, S. G. B., and Bligh, E. W., Sixty Centuries of Health and Physick.
Sudhoff, Karl, Essays in History of Medicine, New York, 1926.
Taylor, Henry Osborn, Greek Biology and Medicine, Boston, 1922.
Thorndike, Lynn, History of Magic and Experimental Science, New York, 1929.
Walton, Alice, The Gult of Asklepios.
Wilkinson, J. Gardner, Manners and Customs of the Ancient Egyptians.
Zeller, Eduard, The History of Greek Philosophy, London, 1931.

PROPOSED INDIANA INTER-PROFESSIONAL HEALTH CONFERENCE.

A preliminary meeting of the Proposed Inter-Professional Health Conference was held in the Union Building, Purdue University, on April 27th, for the purpose of perfecting a tentative program for the creation of an Indiana Interprofessional Health Conference. The purpose of the Conference is to enhance the quality of public health service and to study the various civic, health and professional problems with the view to rendering better health service to the citizens of Indiana.

At the meeting a proposed Constitution was accepted for submission to the various Member-Associations for their consideration and adoption. The following articles are quoted.

ARTICLE I.

Name. This organization shall be known as the Indiana Interprofessional Health Council. The associations herein-after named shall be known as Member-Associations; the individuals, as Members.

ARTICLE II.

Objectives. (*a*) To enhance and protect the quality of public health service and the general public weal of the citizens of Indiana.

(*b*) To provide a clearing house for the interchange of information and knowledge between the Member-Associations, looking toward effective coöperation in the securing and maintaining of the highest professional standards of public health service.

(*c*) To inform the public with regard to the aims of the individual Member-Associations and thus advance the welfare of these respective associations.

(*d*) To furnish a means for study of and research in the various civic, health and professional problems in which the Member-Associations have common interest.

(*e*) To coöperate as a single unit in local, state and national problems and/or emergencies of mutual interest; this to be carried out by means of education of the laity, so that they may thereby be authoritatively informed.

ARTICLE III.

Membership. The membership of the Council shall be composed of five representatives from each of the following organizations: The Indiana State Medical Association, the Indiana State Dental Association, the Indiana Pharmaceutical Association, the Indiana Hospital Association, the Indiana State Nurses' Association, the secretary of the State Board of Health, the dean of the School of Pharmacy of Purdue University, West LaFayette, the deans of the Schools of Medicine of Indiana University at Bloomington and Indianapolis, of the School of Dentistry, Indiana University, and of the Indianapolis College of Pharmacy.

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meeting of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter. *Please advise us of changes in Roster and mail reports promptly.*

CITY OF WASHINGTON.

The regular meeting of the Washington Branch was held at the INSTITUTE OF PHARMACY, April 18th. Minutes of the March meeting were read and approved. Dr. Fuller, chairman of the Program Committee, announced that Dr. C. A. Browne of the Bureau of Chemistry and Soils, would give an illustrated talk entitled "Some Relations of Pharmacy to Alchemy and Early Chemistry in America," at the May meeting.

Dr. W. Paul Briggs, discussing "Pharmaceutical Education in the United States," reviewed the early history from the first pharmacy in Bagdad and the oldest school in Solerno. In early American history, previous to the founding of the first pharmacy in 1770, medicine and pharmacy were combined, the physician usually compounding his own prescriptions.

The first movement to set up a separate school of pharmacy was carried out in 1816 at the University of Pennsylvania; the first degree in pharmacy at this institution was awarded in 1821. The Philadelphia College of Pharmacy and Science was founded in 1821 at Independence Hall in Philadelphia by the apothecaries of the city who were united by the fear of the domination of pharmacy by the medical profession. The curriculum usually consisted of evening courses conducted by the pharmacists themselves to supplant the practical work. There were no science courses. The School of Pharmacy at the University of Michigan was founded in 1876. Now 75% of the schools of pharmacy are either state-supported or endowed institutions.

Entrance requirements were very low between 1821 and the beginning of the 20th century. In 1920, one year of high school was required for admission, in 1931, four years. The course in pharmacy was extended to two years in 1915, to three years in 1922, and to a full four-year course in 1932. The amount of practical experience required of a student varies between states.

The degrees conferred upon graduation are the baccalaureate degree and the degrees of Master of Science and Doctor of Philosophy. Changes are made in the curricula of the schools to keep them abreast of the times. The American Council of Pharmaceutical Education, the Pharmaceutical Syllabus, and the American Association of Colleges of Pharmacy have been formed to guide the expansion and advancement of the profession.

The American Council of Pharmaceutical Education grew out of the practice of individual members evaluating the different schools. The council has adopted standards of education similar to those in the legal and medical professions, and accredits the existing schools according to them. As the standards have been raised, the number of schools has decreased.

The problem of pre-pharmacy training was raised by Dr. Swann and discussed by Dr. Briggs, Dr. Kelly and Dr. Kebler.

"Some Interesting Poison Cases" was the subject of the combined talks of Mr. W. V. Linder and Mr. P. J. Valaer, both of the Internal Revenue Department. Mr. Linder reviewed the

history of the Poison Ginger of Ginger Jake Case from his entrance into the department eight years ago. At this time the Bureau was working on the classification of beverages for governmental taxation. In 1924, fifteen or twenty U. S. P. and N. F. preparations were classed as beverages. Jamaica Ginger had been used for forty or fifty years and its use was increasing rapidly in the South and Southwest before it, too, was classed as a beverage in 1934. The double strength soon followed but the fluidextract, considered unfit for consumption as a beverage, was often adulterated with molasses, glycerine, olive oil or mineral oil.

In February 1930, there appeared on the market fluidextract of ginger which caused paralysis of the wrists and ankles of the consumers. Analysis showed it to contain phenol and phosphates. Dr. Fuller suggested that selindol, a plasticizer containing ortho tricresol phosphate, might have been used as an adulterant; and tests conducted by the Health Department showed that this substance produced the same effect in animals as the ginger preparation.

About 15,000 people, principally boys and girls, were crippled by this "Gig food." The young people quite often recovered from the effects of the paralysis but the older victims did not. There were several firms manufacturing this product, the most important being in Boston. This firm used bootleg alcohol, ginger, ortho tricresol phosphates and diethylene glycol in its product. The ortho tricresol phosphate was used because it took up the ginger and made a nice solution.

Mr. Valaer described the chemical procedure by which pure ortho tricresol phosphate was separated. All of the ginger on the market, about 100 barrels mostly Jake, was seized and to the promptness of this move was credited the saving of roughly 80,000 people from the effects of the poisoning. When the cases were taken to court, victims from every walk of life and many professions came to testify. Dr. Van Itallie corresponded with Mr. Linder and Mr. Valaer with reference to similar cases appearing in Jugoslavia and Austria. It was found that apiol, used in abortions, was being diluted with ortho tricresol phosphate to make it last longer.

The meeting was adjourned at ten o'clock.

KENNETH L. KELLY, *Secretary.*

NORTHERN NEW JERSEY.

The Northern New Jersey Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION met at Rutgers College of Pharmacy April 18th. About 150 attended this meeting, which was the annual Physicians-Pharmacists meeting.

Dr. Reeve L. Ballenger, Member of the Pharmaceutical Problems Committee of the New Jersey Medical Society, spoke on "Professional Relations of the New Jersey Medical Society." Because Dr. Ballenger was a graduate pharmacist before becoming a physician he well understood many of the problems of both professions. Some of the points made by the speaker were: the absence of the professional atmosphere in many of the pharmacies; the failure of the pharmacist to detail, or properly detail, the physician on official drugs and preparations; the failure of the physician to avail himself of the assistance the pharmacist could render.

Mr. William R. Ricart, chairman of the Professional Relations Committee of the New Jersey Pharmaceutical Association, in his topic "The New Jersey Formulary," told of the work that was being done to bring to the physician suitable preparations to meet the needs of the profession. The fact that many of the formulas of the first edition of this booklet were included in the N. F. VI indicates the merit of the booklet.

Dr. Thomas M. Pascall, M.D., a medical practitioner of Newark, in the topic "A Wider Pharmaceutical Knowledge of Official Medication for the Physician," criticized the medical schools for their failure to better equip the students with a knowledge of official medicaments and prescription writing. He also cited many instances of official preparations that were the equivalent of more expensive proprietary preparations.

Professor Adolph F. Marquier, in speaking of "Official Medication and Its Uses," illustrated his talk with many preparations of the U. S. P. and N. F.

Demonstrations of U. S. P., N. F. and New Jersey Formulary preparations were made in the Dispensing Laboratory after the meeting. Students of the senior and junior classes prepared these, and much interest was shown in their work by both the physicians and the pharmacists.

Each year this annual event is attracting more interest from both professions.

C. L. COX, *Secretary.*

NORTHWESTERN.

A joint meeting of the Northwestern Branch of the A. PH. A. and the Scientific and Practical Section of the Minnesota State Pharmaceutical Association was held on Wednesday morning, April 27th, in the ballroom of the Nicollet Hotel, Minneapolis.

Dean Emeritus F. J. Wulling presided over the joint meeting assisted at times by Prof. E. B. Fischer. The following lectures and papers were presented: "The Romance of Spices," by G. Demars; "Seeing Ourselves," by Roy Paulson; "The Professional Pharmacist," by Sister M. Constance; "Chairman's Address," by F. J. Wulling; "Sistosan, a Non-Toxic and Non-Irritant Hæmostatic," by Sister St. George; "THE INSTITUTE OF PHARMACY or the Headquarters Building of the A. PH. A., at Washington, D. C. (illustrated)," by Prof. E. N. Gathercoal, president of the A. PH. A.

A second joint meeting of the two bodies convened Thursday morning, April 28th, in the same place to listen to the following program: "Andrew J. Kline, a Memoir," by F. J. Wulling; "The Pharmacist and Public Health," by N. Vere Sanders; "Factors Influencing the Stability of Liquor Magnesii Citratis U. S. P. XI," by George E. Crossen and Dean Chas. H. Rogers. "The 1938 A. PH. A. Meeting in Minneapolis," by F. J. Wulling; "Dispensing Problems," by Gustav Bachman; "Correlations of Predictive and Achievement Tests Given to Students Entering Pharmacy," by Dean Chas. H. Rogers; "The Chemotherapy of Blood Infections," by Miss Laurine Jack; "Drugs Affecting Blood Pressure," by Prof. Glenn L. Jenkins; "Sodium Perborate as a Toothpowder," by Chas. V. Netz; "The Pharmaceutical Aspect of Cannabis," by Prof. E. B. Fischer; "N. F. Revision and Research Work," by Prof. E. N. Gathercoal; "Public Health," by Prof. Gustav Bachman; "Nostrums, Old and New," by C. E. Smyithe; "The Future of Pharmacy, 1912 *versus* 1937," by R. Messing.

Chas. V. Netz, secretary-treasurer of the Northwestern Branch of the A. PH. A., presented his official report for the past year. He called attention to the coming 1938 convention of the A. PH. A. to be held in Minneapolis in August, pointed out that all Minnesota Pharmacy would be host to the convention guests and promised a campaign for A. PH. A. membership among the Minnesota pharmacists within the next month.

CHAS. V. NETZ, *Secretary-treasurer*, Northwestern Branch of the A. PH. A.

ABSTRACTS OF CONTRIBUTIONS TO THE MEETING OF THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCES.

The Subsection on Pharmacy was held on December 27th at ten o'clock in the ballroom of the Antlers Hotel, Indianapolis, Indiana. Below are given the abstracts of the papers that were delivered in that Section.

1. *The Assay of Midriatic Drugs.*—Alice Hayden, C. B. Jordan and H. G. DeKay. The authors determined the quantity of volatile constituents in hyoscyamus, belladonna and stramonium. These constituents were tested pharmacologically and certain assay processes checked and modifications of the official assay processes for midriatic drugs and preparations were recommended to the Rivision Committee of the United States Pharmacopœia.

2. *Homologs of Salol. The Salicylates of Isomeric Amyl Phenols and Amyl Cresols.*—H. G. Kolloff, J. O. Page and M. C. Hart. Since the establishment of the salol principle by Nencki, several esters of salicylic acid have been prepared in the hope that they would display a more powerful internal antiseptic action than the phenol salicylates. The discovery that the alkyl substituted phenols and cresols are more germicidal than the unsubstituted ones raises the question of whether or not salicylates of these might be more efficient internal antiseptics than salol. The salicylates of the following phenols were prepared by refluxing the desired phenol and salicylic acid in toluene with phosphorus oxychloride: *o*-*n*-amyl phenol, *p*-*n*-amyl phenol, 3-*n*-amyl-*o*-cresol, 5-*n*-amyl-*p*-cresol, 4-*n*-amyl-*m*-cresol, 3-*n*-amyl-*p*-cresol, sec.-amyl-*p*-cresol and 4-chlor-*o*-cyclo-hexylphenol. The rate of hydrolysis of these esters was found to compare favorably with that of salol.

3. *The Chemical Constitution and the Physiological Activity of the Latex of Ficus pumila L.*—Conrado F. Asenjo. *Ficus pumila* L., also known as creeping fig, has not been previously

investigated phytochemically. The author gave an account of the investigation now under way, on the chemical constitution of this latex. A protein fraction obtained from the latex exhibits the property of digesting some human and animal parasitic worms.

4. *A Study of the Toxic Principles of Red Squill.*—Floyd J. LeBlanc and C. O. Lee. Red squill powder is very toxic to rats but not so toxic to other forms of animal life. The active toxic principle has not been definitely isolated, but an alcohol-ether solution was obtained which when evaporated gave no definite melting point but was found to be approximately one hundred times more toxic than the original red squill powder. White female rats are killed by one-half the dose necessary to kill white male rats.

5. *Gelsemicine, Aconitine or Pseudaconitine; Which Is the Most Toxic Alkaloid?*—K. K. Chen, Robert C. Anderson and E. Brown Robbins. The toxicity of gelsemicine, aconitine and pseudaconitine (in form of their halides) was compared, weight for weight, in mice, rats, guinea pigs and rabbits. The alkaloids were injected intravenously in mice, rats and rabbits, but subcutaneously in guinea pigs. The order of toxicity of the three substances varies from one species to another. The results show that in mice, gelsemicine > aconitine > pseudaconitine; in rats, gelsemicine > pseudaconitine > aconitine; in rabbits, pseudaconitine > aconitine > gelsemicine; and in guinea pigs, pseudaconitine > aconitine > gelsemicine.

6. *Daphnia—Indicator and Dosimeter in Microphysiology.*—Arno Viehoever. Experimental work with daphnia shows that it can be used as an indicator on organs representing the muscular, nervous and glandular tissues in the case of many hypnotic irritant and laxative drugs as well as snake venoms and insecticidal substances.

7. *Mechanism of Action of Alpha Naphthyl Isothiocyanate.—A New Organic Insecticide.* A. Viehoever and N. Tischler. A 1 per cent solution of alpha naphthyl isothiocyanate in combination with 0.03 per cent of pyrethrins in kerosene gives excellent control of house flies; a 2 per cent solution of the chemical alone in kerosene when used at the rate of 1 pint to 1 quart on 100 square feet of the usual upholstery, woolen fabrics will give good control of clothes moth larvæ and a tripple amount of this mixture will give good control of carpet beetle larvæ. The speed action, where it is essential for practical purposes, can be greatly hastened by the addition of small amounts of pyrethrum extract.

8. *Enteric Coatings.*—J. T. Goorley and C. O. Lee. The studies showed that the commonly used enteric coatings are unreliable. A coating mixture was devised which depended upon the action of the digestive enzymes for disintegration. A new formula was given with the procedure of applying it and the reliability of the coating was shown by numerous X-ray pictures and fluoroscopic experiments.

9. *Field Tests for Marihuana (Cannabis).*—Arno Viehoever. Tests were designed for the immediate analysis of cigarettes or leaves in case of seizures which were supposed to contain marihuana. The most rapid extraction of the narcotic principle, cannabinol, without the excessive interference of plant pigments, can be made by placing the contents of $^1/_4$ of a marihuana cigarette ($^1/_{300}$ ounce) in the reagent benzene (9 parts) and 2 per cent alcoholic potash (1 part) for 5 seconds. This reagent is rapidly poured off into a low-mouthed glass receptacle. From $^1/_2$ to $1^1/_2$ minutes the yellowish tint changes to pink and a deeper red, leaving after evaporation a purple residue. The residue redissolved in acetone yields a bluish violet tint, while in strong ammonia an orange-red coloration appears. Using the benzene solution of marihuana (extracted for one minute) when evaporated and then tested on transparent Daphnia magna, the biological reagent, supplementary physiological evidence of unmistakable narcosis is obtained within one hour. Frost apparently does not destroy the activity of the agent.

10. *The Effect of Peptone on the Resistance of Staphylococcus aureus.*—George F. Reddish and Ella M. Burlingame. Ten peptones were studied as to their effect on the resistance of *Staphylococcus aureus* to germicides. Then tested on the third, seventh and tenth days after transfer to broth made with each peptone, differences in resistance of these cultures were observed. Since tests on phenol dilutions were made at five, ten and fifteen minutes these variations were not so apparent as when the cultures were tested on an antiseptic solution at time intervals of thirty seconds, one, two and three minutes. When these shorter time intervals were employed in the tests it was shown that nine of the ten peptones gave weaker cultures than did the broth made with Armour's peptone. These results showed that Armour's peptone in our hands was best

suited for use in media employed for growing *Staphylococcus aureus* for use in testing antiseptics and disinfectants.

11. Fluorescence Analysis of Some Alkaloids and Crude Drugs.—Abraham Slesser. The substance or substances causing the characteristic fluorescence of alcoholic extracts of ipecac in ultraviolet light is alkaloidal in nature. The elimination of other alkaloids by using the proper precipitants seems to show that either psychotrine or *o*-methyl psychotrine, or both, are apparently found responsible for the fluorescence found in alcohol extracts of ipecac.

12. The Determination of Volatile Oil in Vegetable Drugs.—Elmer H. Wirth. A study was made of the various methods for the determination of the amount of volatile oil in vegetable drugs. The efficiency of the various methods was determined and experimental evidence was obtained illustrating the sources of error in the volatile ether extract method in the United States Pharmacopœia. The study is of value in revising the methods used in pharmacopœial revision.

13. The Glycosides of Asclepias Cornuti or the Common Milkweed.—A. H. Rihn and H. G. DeKay. This plant has been studied for its caoutchouc content. Glycosides and saponins have been found in other species of Asclepias. The commonly accepted methods of extracting the drug was used and any glycosidal material was isolated from the extracts of the leaves, the stems and the rhizomes. It was found that the sugars, sucrose and glucose, were present in the aqueous and alcoholic extracts of the several portions of the plant. The leaves and stems yielded a bitter principle which was divided into two fractions, one possessing toxic properties and the other non-toxic. There was apparently no glycoside in the leaves and stems. A glycoside was found to be present in the rhizomes which produced toxic principles when injected into sparrows.

Joint Session of the Subsection on Pharmacy with the Section on Medical Science was held on Monday, December 27th, 2 P.M., at the Antlers Hotel. The papers presented are abstracted as follows.

1. Inhibitions of the Autonomic Nervous System Which May Enter through the Eyes.—E. L. Jones. The author discussed abnormal mechanisms in the eyes as causative factors in the production of numerous symptoms in other parts of the autonomic nervous system. A large number of clinical cases was cited as evidence.

2. Influence of an Anterior Pituitary-Like Principle on the Growth and Function of the Genitalia of the Male.—W. O. Thompson, N. J. Heckel, P. K. Thompson and L. F. N. Dickie. The anterior pituitary-like principle from the urine of pregnant women exerts a profound influence on the growth and function of the male genitalia. It is much more efficacious in the production of genital growth in man than any extract of the pituitary itself which is available at present. In young boys it may produce such marked stimulation of genital growth that premature puberty results. Boys developing premature puberty from the use of this material show a marked increase in the size of the penis, scrotum and prostate and the amount of pubic hair. In contrast to these changes the testes show little or no increase. Susceptibility to this growth stimulus is greater before than after the age of puberty, but is not completely absent after this period, a marked increase in the size of the genitalia having been produced with large doses as late as the age of thirty-seven years. The genitalia stops growing and may decrease in size when the administration of this material is discontinued. Because of its stimulation of genital growth, it is valuable in the treatment of hypogenitalism in the male, particularly in the boys of the Fröhlich type, and facilitates the operative correction of hypospadias.

3. Leukæmia: Its Etiology, Nature and Cure in Animals. Its Possible Relations to Certain Specific Diseases of the Human.—M. W. Emmel. Leukemia has been induced in the chicken, dog, monkey, hog, sheep, goat and mouse by the repeated intravenous injection of small numbers of bacteria of the paratyphoid and typhoid groups. Such infection if carried to a certain point results in a chronic but progressive process of tissue autolysis without further stimuli by the causal organism. This fundamental process of self-perpetuating autolysis of blood tissue eventually leads to the development of leukemia in from two to nine months. This process of progressive tissue autolysis can be initiated not only by the viable causal organism but also by similar injections of heat-killed causal organisms, chemicals, such as benzene, phenol and xylol, and homologous tissues (dog tissue into the dog, monkey tissue into the monkey, etc.). The nature of the fundamental process of tissue autolysis is similar regardless of the agent initiating the process and the species involved. An homologous tissue antiserum will cure the major portion of cases of all

types of leukemia in the chicken and lymphatic leukemia in animals. The process of progressive tissue autolysis offers a new avenue of approach to the study of cancer and possibly other diseases of man and animals.

4. Chronic Rheumatic Brain Diseases as a Factor in the Causation of Dementia Præcox.—Walter L. Bruetsch. Eight per cent of dementia præcox patients who were examined at autopsy showed signs of a chronic rheumatic infection, affecting the brain as well as the heart. In a small number of cases it was known that the infection had damaged the heart. The rheumatic affliction of the brain, however, which caused the mental breakdown was not suspected and was not recognized while living. The suggestion is made to separate the cases of dementia præcox caused by rheumatic brain disease from the large descriptive group of schizophrenia as a subgroup with a distinct etiology.

5. Investigation on Certain Basic Mechanisms Necessary for Complement Activity.—E. E. Ecker. The study showed a close parallelism between ascorbic acid content and the activity of fresh guinea pig complements. Serums of scorbutic guinea pigs showed low complementary activities. The parallelism held true up to 1 mg. of ascorbic acid per 100 cc. of serum at which point no further increase of ascorbic acid in the blood serum of guinea pigs and in the case of subacute scurvy a rise of complementary activity was found. The effect of ascorbic acid on various fractions of complement was investigated and finally the effects of oxidizing agents like iodine, quinone, H_2O_2, O_2, Cu_2O, C_6H_5HgCl and von Szent Györgi's hexoxidase. Under controlled oxidation studies we were able to reactivate the weakened complement by means of several reducing agents like ascorbic acid, H_2S, $Na_2S_2O_4$ and KCN. Aged complement was markedly reactivated with H_2S water. A study just completed introduces the relation of glutathione content of whole blood and complementary activity of the serum. It is possible to markedly reduce the glutathione content of the whole blood of guinea pigs and rabbits but the fall of complementary activity was not marked as in the case of scorbutic animals. In the animals with reduced blood glutathione contents the ascorbic acid was maintained at a normal or higher than normal level.

6. Desiccated Thyroid Feeding and Androgenic Function of Ovaries.—R. T. Hill. Male mice were castrated and at the same time received grafts of mouse ovaries in their ears. Subsequently the animals were subjected to an environmental temperature of 20° C. for several weeks, after which time their sex accessories had returned to normal as a result of the androgenic function of the grafted gonads. A second period of treatment consisted of continued exposure to 20° C. temperature plus the daily feeding of a non-toxic amount of desiccated thyroid tissue for 21 days. At the end of this period of thyroid feeding the gross appearance of the sex accessories was that of long castrated males. Normal control males, kept under identical temperature and feeding conditions did not show any loss in the androgenic function of the testes as exhibited by the seminal vesicles and prostates. In a castrated male carrying an androgen secreting ovarian graft it is concluded that in some manner the feeding of thyroid enters into the local or general metabolism (or chemism) to block or inactivate continued androgenic function of the grafted gonad. Since no similar response was obtained in the normal males, it is suggested that the androgen (*s*) secreted by a grafted ovary is of a different chemical nature than that of the testis.

7. The Problem of Evaluating the Clinical Activity of Ergot Preparations.—Marvin R. Thompson. The assay methods officially enforced in the United States, Canada, Great Britian and other countries, measure chiefly the ergotoxine group of ergot alkaloids which are responsible for but a small part of the oral clinical activity, while completely neglecting the ergostetrine activity which is responsible for the greater part of the clinical activity of Pharmacopœial Ergot preparations.

8. The Local Anesthetic Action of Thiazoles, Oxazoles and Imidazoles.—Charles L. Rose. Four groups of new synthetic local anesthetics have been investigated in animals and in man. They are chemically derivatives of benzothiazole, dihydrothiazole, dihydro-oxazole and imidazole. A most interesting finding is the fact that a member of the series has a very low toxicity by intravenous injections (approximately 40 per cent lower than that of procaine) but a higher toxicity by subcutaneous injection (approximately 100 per cent more than that of procaine).

9. The Hemolytic Action of Sodium and Potassium Soaps.—Leroy D. Edwards. There are no chemical tests that will satisfactorily distinguish true olive oil soap from soap made from other oils. A study of the mechanism of the hemolytic action of sodium and potassium soaps was undertaken as a possible means of determining the nature of the soap. Chemically pure soaps were

prepared from each of the following acids: lauric, myristic, palmitic, stearic, oleic and ricinoleic. The hemolytic power of these soaps was then determined at various H-ion concentrations over a p_H range of 6 to 9. The effects of the addition to a soap solution of alkali, mineral acid and free fatty acid were also investigated. The results obtained in the p_H study indicates that the typical hemolytic curve of a soap shows in the extreme acid range only moderate hemolytic power. As the H-ion concentration is reduced, the lytic value is lowered. The maximum values of the different soaps occur at widely differing p_H ranges. These results also demonstrated that the determination at 37° C. of the complete lytic curve for most soaps is impossible since the rise and fall of the curve do not come within the p_H limits of stability of the human red cell. The rises and succeeding falls in the hemolytic curves of the more soluble soaps appear at a higher H-ion concentration than those of the more insoluble soaps. When the soaps of the saturated fatty acids are compared as to their greatest lytic values at a given temperature, the following order is found: laurates > myristates > palmitates > stearates. This order does not hold at a given p_H. At a given p_H, an increase in the temperature enhances the hemolytic action of soaps. The following factors as possible causes for the observed augmentation and diminution of the hemolytic value of a soap at various p_H ranges are suggested: (1) the lowering of surface tension by soap; (2) the free alkali of soap solutions; (3) undissociated soap; (4) free fatty acid; (5) fatty acid ion; (6) acid soap. The conclusion is made that the ultimate lytic component of common soap solutions is the fatty acid molecule, and that it is enabled to act as such through the mechanism of some intermediate product of hydrolysis such as the acid soap or through a peptizing effect of undissociated soap.

10. Mechanism of Action of Aphrodisiac and Other Irritant Drugs.—Arno Viehoever and Isadore Cohen. There is need for the selection and evaluation of an efficient but safe aphrodisiac. Therefore a study of certain aphrodisiac drugs was undertaken. In the initial studies, Daphnia magna, the transparent crustacean, was selected as a test animal since it had previously shown its merit as a biological reagent in the specific action and associated effects of drugs, especially narcotics, laxative substances and potent poisons. Both the specific action and the associated physiological effects of the following three substances were recorded: yohimbine (HCl salt), cantharidin and capsicin. All three substances cause pronounced and continued excitatory movements of the male genital organ. Actual ejaculation of the sperm was observed with the use of cantharidin. In varying concentrations the order of increasing lethal toxicity was found to be yohimbine, capsaicin and cantharidin. These agents in high concentration also produce irregular clumping and stasis of the intestinal contents as a result of the progressive and prominent swellings in the lining of the intestinal canal. In low concentration, 0.0033–0.0025%, yohimbine causes evacuation in young daphnia (7–9 days old); while capsaicin and cantharidin, both 1:30,000, show as a rule no indication of valuable laxative properties, their local irritant action apparently prevailing. Yohimbine and capsaicin in varying concentration depress progressively both the heart, producing dilation, and the respiratory movements. Cantharidin in suspension stops first, all vital activity except that of the heart, which then shortly collapses. Gravid females exposed to 0.1–0.025% yohimbine for five hours can be recovered by returning them to culture media although there remains even after 24 hours a partial depression of the heartbeat. Normal life activity, including the release of several broods of young, was observed subsequently. Yohimbine and capsaicin in varying concentration produce an exaggerated torsion of the muscles controlling the movement of the eye. Paralysis of these movements occurred after one hour in a suspension of capsaicin. The alteration in the normal swimming of animals under the influence of yohimbine (0.2–0.025%) and capsaicin (suspension) is caused by the incoördination of antennal movements, and, possibly in part, by the derangement in the optical system. The derangement of the swimming mechanism and the internal disturbances correlated can obviously be used as criteria in establishing the toxicity of test substances. These results with Daphnia furnish additional evidence that there are no sharply demarcated physiological differences between invertebrates and vertebrates. Certain specific and associated effects coincide with previous findings on vertebrates. The value of Daphnia as a biological reagent is further demonstrated by the unmistakable and consistent response of the anatomical and physiological systems to these additional test substances.

11. Light Deficiency Rickets in Monkeys (Macaca rhesus).—Henry J. Gerstenberger. On the basis of observations made on a total of 48 monkeys, protected against exposure to antirachitic wave-lengths and receiving a diet high in phosphorus as compared with calcium, it is concluded

that the rickets produced is quite like that met with in full-term human infants, inasmuch as 47 developed in the blood a low phosphorous level and only one a low calcium level.

12. New Pharmacological and Bacteriological Facts about Iodocholeates.—Paul C. Goedrich. It has been found that the germicidal properties of iodocholeates are superior to those of tincture of iodine when tested under severe and generally unfavorable conditions. Both aqueous and alcoholic solutions of iodine combine rather rapidly with blood serum, the iodine thus combined possessing no germicidal properties. Iodocholeates in solution combine with blood serum to a very much smaller extent, and for this reason its germicidal action is not reduced as appreciably as aqueous or alcoholic solutions of iodine, when used under conditions where blood serum and tissue fluids are present as is so frequently the case in general use. The free iodine in a tincture or Lugol Solution is rapidly converted into iodocholeates when bile acids or their salts are added. This reaction is followed by a marked increase in germicidal action. Iodocholeates are but very slightly volatile at body temperature. A 2 per cent solution of iodocholeates will retain many times as much iodine as a 7 per cent U. S. P. tincture after exposure of 10 to 15 minutes at such temperatures. An alcoholic solution of iodocholeates when boiled shows no separation and almost no volatilization of iodine. Further tests again indicate the exceedingly low toxicity of iodocholeates. The fact that iodocholeates retain their iodine in active form under conditions such as exist in the treatment of wounds is of clinical significance. Its low volatility prevents the loss of iodine such as has been found to occur in the case of the U. S. P. tincture. Because of the fact that it is non-irritating, it can also be used under bandages without causing blistering or other bad effects.

13. A Study on the Temperature Necessary to Cause Death in Fatigued Neurons as Compared with Resting Neurons.—George D. Shafer and Royce K. Skow. It has recently been shown that the heat rigor temperature of fatigued muscle is considerably lower than that of resting muscle, the lowered rigor temperature of fatigued muscle cells being associated with their uptake of water through an increased osmotic pressure which they acquire during the fatiguing process. It is now shown that when fatigued and resting neurons and nerve fibers (mates) are heated at once, the heated units lose irritability at a slightly lower average temperature and are killed at a very slightly lower average temperature than their resting mates, the death temperature being a little higher in every case than the temperature at which irritability is lost. When fatigued and resting neurons or nerve fibers have been heated until all irritability has been lost, but not to the killing temperature, they recover on cooling, but sensory resting units recover an action potential averaging 4.3 times greater than that of their fatigued mates; the resting motor fibers 3.0 times higher than their fatigued mates. The average differences in temperature at which irritability is lost and at which death results in fatigued and resting nerve units, though small, are shown to be significant by Fisher's method of analysis of variance. It is suggested, by analogy with results on muscle, that the above temperature differences with respect to fatigued and resting neurons may be associated with uptake of a slight amount of water by the fatigued units.

DRUG PRICE RESEARCH PLANS ARE LAID.

The executive committee of the National Association of Retail Druggists and the board of control of the National Wholesale Druggists' Association have each approved the expenditure of $5000 to establish a fund to be used by the Druggists Research Bureau in assembling facts concerning trends in consumer prices since the enactment of fair trade laws.

The present delegates are N. A. R. D.—John W. Dargavel, Chicago; Thomas Smith, Wilmington; and George L. Secord, Chicago; N. W. D. A.—A. Kiefer Mayer, Indianapolis; Leo A. Lanigan, Chicago; J. T. Woodside, Chicago; H. S. Noel, Indianapolis; and E. L. Newcomb, New York City; A. A. C. P.—George C. Shicks, Newark; W. Henry Rivard, Providence; and Paul C. Olsen, Philadelphia.

EDUCATING THE PHYSICIAN AND THE PHARMACIST REGARDING OFFICIAL TYPE OF PRESCRIPTIONS *VERSUS* THE PROPRIETARY TYPE.*

BY FRANK A. DELGADO.[1]

The extent that proprietary, trade-marked prescription specialties are prescribed is a subject of international concern. From Germany it is reported that the retail pharmacist finds his sphere of activity greatly hemmed. Trained and destined by tradition to be essentially a prescription druggist, *i. e.*, to fill prescriptions of physicians from ingredients carried in stock, he finds that a large per cent of his sales represents packaged, trade-marked and patented preparations sold at a prescribed maximum price. These preparations, however, offer an irresistible fascination to the physician because of the convenience in prescribing them.

The situation in Germany has become so acute that in 1936 the German Government met with representatives of the German pharmaceutical industry and pharmacists in order to iron out certain points of discord between the two groups. It is reported that as a result of this meeting, the pharmaceutical industry will keep a record of any specialties and agree to reduce the number of the various sizes of packages and to make other concessions required by the pharmacist.

The spread of health insurance throughout the world is focusing attention on the subject of proprietary and official prescription ingredients. This could not be better illustrated than in a report recently received from England stating that "the bulk of the medicines supplied to insured persons in England under the national health insurance scheme are of the official or semi-official pharmacopœial type, less than 2 per cent of the prescriptions being for proprietary preparations. The British Medical Association has issued a national formulary designed to supply practitioners with a compendium of prescriptions of pharmacopœial type and to discourage the use of proprietary preparations when non-proprietary preparations of analagous therapeutic effect are available.

In nearby Canada, there is seldom a meeting of pharmacists that the subject is not brought up in one form or another resulting in statements such as:

"Look through your prescription file and then ask the Medical Profession how under the name of Heaven, if he enlists himself to prescribe all these proprietary specialties, can the dispensing druggist do otherwise than obey his orders and how can he do otherwise than charge a high price when the expensive detail, free samples and high pressure advertising have all been included in the cost."

And again, in a paper by Ivon Garcia of North Vancouver, B. C.:

"There can be no doubt that the advent of mass production as applied to pharmaceutical operations has taken away a large portion of what was once magistral pharmacy."

As recently as July 15, 1937, in an article entitled "Turnover and Its Relation to Margin," E. O. Houghton of Toronto states:

"It seems to me that it would be well to encourage physicians to write legitimate prescriptions rather than write these semi-patents, which you sell over the counter and on which you make

* Section on Education and Legislation, A. PH. A., New York meeting, 1937.

[1] Business Specialist, Bureau of Foreign and Domestic Commerce, Department of Commerce.

no profit. We often have to open a package and dispense half a box and we lose money due to obsolescence."

I do not necessarily agree with some of the aforementioned statements and quotations originated abroad and only mention them to show that the subject is one of importance to pharmacists throughout the World.

One has only to examine the proceedings of the National and State pharmaceutical associations in this country to find that it is also receiving considerable attention in the U. S. For example, at the last meeting of the New Jersey State Pharmaceutical Association, the following resolution was referred to the Committee on Professional Relations:

"*Resolved*, That the New Jersey Pharmaceutical Association asks the coöperation of all pharmaceutical manufacturers to cease bringing on the market any new compounds or specialties using the common every-day U. S. P. and N. F. drugs.

"*Resolved*, That the Professional Relations Committee be empowered to use their own judgment in calling attention of the Council of Pharmacy and Chemistry of the A. M. A., to numerous duplications of prescription proprietaries."

While he was probably not speaking exclusively of prescription proprietaries, nevertheless the comment of H. J. Ostlund, Statistical and Cost Accounting Expert of the National Wholesale Druggists' Association is not irrelevant. Mr. Ostlund stated at the September 15, 1931 meeting of the Drug and Chemical Section of the New York Board of Trade:

"The channels of distribution were choked with slow-moving competitive proprietaries."

Two resolutions were presented at the 1936 meeting of the National Retail Druggists' Association:

"Asking the Association to confer with manufacturers in an effort to correct the duplication of pharmaceuticals by different firms" and "Asking the Association to file protests with manufacturers against the packaging of simple admixtures of common drugs and chemicals as finished prescriptions and detailing them to physicians under composite trade names."

In a discussion of this kind, the question naturally arises: Are there any facts and figures that will throw any light on the subject? The answer is Yes. The attention of anyone interested in studying the subject further is directed to that part of Chapter III on page 29 of "The Professional Pharmacy" (one of the National Drug Store Survey Reports) entitled "Average Cost of Materials and Selling Price of Prescriptions." The facts revealed in Tables XVI, XVII and XVIII should also prove of interest.

One will see upon examining these tables, that the average selling price of an official prescription is from 78 cents in Store 6B to 96 cents in Store 4C whereas the average selling price of the specialty type prescription is from a low of $1.00 in Store 6B to a high of $1.16 in Store 11B. There is probably an average difference in cost to the patient of 20 per cent or more for the country as a whole and when you stop to think that at least 165,000,000 prescriptions are filled annually in the United States of which at least 40,000,000 are of a specialty or proprietary or non-official character, you can see that the physicians could save their patients literally millions of dollars annually if they prescribed more official and less non-official ingredients and preparations.

Not only in the chapter just mentioned, but throughout the Report will be found factual information dealing with the subject.

There is another angle of this subject which pharmacy leaders throughout the country seem to overlook and that is that without filling a single additional prescription, the pharmacists of the country could make several million dollars more gross profit annually if a substantial portion of specialty prescriptions could be converted into the official type. One is again referred to the aforementioned tables which show that the average official prescription costs the pharmacist from 17 cents to 21 cents whereas the average specialty prescription costs him from 43 to 47 cents. The difference is even greater than these figures indicate for the reason that the turn-over is much greater for official preparations and the investment nowhere near as large.

The May 1937, issue of *The New Jersey Journal of Pharmacy* speaking of these particular facts said as follows:

> " 'The Professional Pharmacy' points out that at least twenty-five per cent of the prescriptions annually filled in this country call for manufacturers' specialties and various proprietary and non-official preparations and that the average difference in cost to the patient on such prescriptions is an increase in price of twenty per cent.
>
> "Thus, in New Jersey alone, where nearly six million prescriptions were filled during 1935 it is estimated that physicians could have saved their patients some $300,000.
>
> "It costs the pharmacist nearly twice as much for the ingredients to prepare the average specialty prescription and he must carry on his shelves at a large investment a great many duplicates for which the turnover is much less than for his stock of official preparations.
>
> "The consumer insists on his right to correct information on the cost and quality of the commodities he uses. His ignorance is being reduced by education and in his enlightenment, he is learning the significance of the terms U. S. P. and N. F. and further, that there is no scientific justification for many proprietary remedies. The consumer will resent the fact that high-pressure salesmanship has stepped-up the cost of the medicines ordered for him. Perhaps when he is brought to realize that the average price of his prescriptions, of which there are some 165 million compounded annually, could be reduced from $1.00 to $.80, he will help the pharmacist in his endeavors to interest the physician in prescribing U. S. P. and N. F. products instead of similar products with trade names."

There is still another angle of the subject that is also rather unpleasant from the viewpoint of the prescriptionist and that is so many proprietary prescription specialties evolved into "over the counter" proprietary medicines not differing particularly from a profit standpoint to numerous drug and toilet preparation loss leaders. One has only to observe the contents of a drug or department store window to see displayed at drastically cut prices a number of proprietary prescription specialties.

The basis of reasoning of certain pharmacists is sometimes incomprehensible. I remember some time ago reading an article by the proprietor of a drug store in which the author stated that new proprietary prescription specialties were responsible for the bulk of his prescription profits, and the proof of this was in the already large and constantly growing number of specialties on his shelves.

One of the most fallacious theories under which a pharmacist could labor is that those items in his prescription stock representing the bulk of his investment likewise are responsible for the bulk of his profit. According to the National Drug Store Survey, proprietaries are responsible for from 35 to 45 per cent of the total prescription department inventory investment, although only accounting for 20.5 per cent of the total number of ingredients used in filling prescriptions. The pharmacist can better judge the importance of his various prescription items, according

to the extent to which they are prescribed, rather than the extent to which his money is invested in them.

There is, of course, without any question a tremendous number of proprietary prescription products. About three years ago, a book was published entitled "Modern Drug Encyclopedia and Therapeutic Guide" listing 8160 modern non-pharmacopœial drugs, chemicals and preparations. It was hardly off the press when the publishers announced the publication of a quarterly supplement. During the past three years, 500 new products have been described in the supplements. The publishers now announce a new volume to be issued in 1938 containing these 500 products and many not previously described. The aforementioned statistics regarding the number of proprietary specialties became all the more interesting when compared with the number of official items listed in the current editions of the U. S. P. XI and N. F. VI which I understand amount to 569 in "The Pharmacopœia" and 689 in "The National Formulary."

Answers to the following questions regarding official and specialty type of prescriptions will be found in "The Professional Pharmacist."[1]

Answers to Questions, Chapter I:

(1) Are specialty prescriptions supplanting official prescriptions? (Page 17.)

Official prescriptions decreased only 2.2 percentage points from 1910 to 1930 while specialties also showed a decrease of 1.3 percentage points in the same period and prescriptions consisting of a mixture of specialty and official ingredients increased 3.5 percentage points.

(2) How do the number of specialty prescriptions compare with official type? (Pages 17 and 18.) Approximately 25 per cent or slightly less than one out of 4 prescriptions call exclusively for specialties. From 50.9 per cent to 53.6 per cent call for official prescriptions and the remaining percentage consist of the mixed type of prescription, *i. e.*, a combination of specialty and official ingredients.

Answers to Questions, Chapter III:

(1) Are high-priced prescriptions usually the official or specialty type? (Page 26.) Nearly $^2/_3$ of the regular prescriptions studied during the National Drug Store Survey and priced at more than $2.00 were manufacturers' specialties, specialties also accounting for the largest proportion of the prescription price at from $1.55 to $2.00. Two-thirds of the prescriptions priced at less than $0.50 were official prescriptions.

(2) Why must the pharmacist charge more for specialty prescriptions? (Page 26.)

The average cost of ingredients in specialty prescriptions was $0.45 as compared with $0.17 for ingredients in official prescriptions. The report states further that "Due to the fact that specialties are responsible for a majority of items in frequent prescribing, they should bear an even higher mark-up."

(3) Has there been much change in prescription prices during the last 25 years and what are the factors responsible for this change? (Page 27.)

Only 2 per cent of prescriptions studied for 1910 were priced at more than $1.00. In 1930 over 21 per cent were priced at more than $1.00. This difference is due in part to the difference in the purchasing power of the dollar in 1910 and 1930. Also in 1910 there were as many high-priced specialties being prescribed.

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[1] Obtainable for 25 cents per copy from the AMERICAN PHARMACEUTICAL ASSOCIATION, 2215 Constitution Avenue, N. W., Washington, D. C.

(4) What type of prescription costs the pharmacist least—narcotic or non-narcotic and why? (Page 29.)

The cost of ingredients in the average narcotic prescription is less than in non-narcotic prescription. One reason is that they are generally prescribed in smaller quantities. Another reason is that there were few specialties among the narcotic prescriptions studied.

(5) Why is it that the cost to the pharmacist of prescriptions varies? (Pages 29 to 32.)

Tables XVI, XVII and XVIII show that this variation is due largely to the extent that a store fills or does not fill specialty type of prescriptions.

Answers to Questions, Chapter IV:

(1) Is there any factual data regarding the preference of physicians for official or specialty preparations? (Pages 39 to 42.)

According to the Report, both "Post-War" and "Pre-War" physicians have a preference for official remedies although "Post-War" physicians have a tendency to mix official ingredients with specialties more than "Pre-War" physicians, do.

Answers to Questions, Chapter V:

(1) How many different ingredients or items will be found in the average drug store? (Pages 46 and 47.)

It was found that 1186 different items were prescribed per 10,000 prescriptions in professional pharmacies and 1274 different ingredients per 10,000 prescriptions in the usual type of drug store.

(2) What proportion of the ingredients necessary to fill prescriptions are official and what proportion are specialty? (Page 46.)

Chemical ingredients amount to less than $^1/_5$ of the total number of different ingredients, but what is more important, they are prescribed about as often as galenicals and specialties combined. Chemical ingredients have the least and specialties the greatest chance of becoming "shelf warmers."

(3) What type of ingredient, official or specialty, necessitates the pharmacist adding to his inventory? (Pages 47 and 48.)

Table XXIX of the Report shows that infrequently used ingredients were developed for a total of 2490 times in 20,000 prescriptions. When a physician wrote an item on his prescription blank, over 94 per cent of the cases, that item was one of a minority group.

(4) Does a pharmacist ever complete his prescription department stock? (Pages 51 and 52.)

This does not seem possible. A study of 20,000 prescriptions, Table XXXIII, shows that 328 different ingredients were required in filling the first 500 prescriptions. In the next 500 prescriptions, 121 new ingredients were required. Even after filling 5000 prescriptions, when the pharmacist might think he had built up a widely assorted stock of prescription ingredients, 34 new ingredients are required. With each succeeding lot of 500 prescriptions, the number of new ingredients required generally diminishes, but even in the 20th block, 10 new ingredients were

prescribed. Chemicals were minor offenders and in the emergence of new ingredients shown in Table XXXIII, had a tendency to emerge in fewer numbers in each succeeding block than either galenicals or specialties. As a matter of fact it was not necessary to purchase any new chemicals at all in the 16th and 17th blocks, and only twenty new chemicals at an average value of $0.57 each for the 1500 prescriptions contained in the 18th, 19th and 20th blocks. On the other hand, it was necessary to purchase 62 new galenicals at an average cost of $0.88 each, and 61 new specialties at an average cost in excess of $1.00 each for the 2500 prescriptions contained in the last 5 blocks of prescriptions enumerated.

(5) Does any information exist regarding items in the prescription department with and without movement? (Page 53.)

The Report shows that of 1451 different items in the prescription department, 513 items (35.4 per cent of the 1451 items stocked) showed no movement of any kind during the survey year. Of these 513 items, 78 valued at $21.00 were chemicals, 241 valued at $131.00 were galenicals and 128 valued at $115.00 were specialties.

Answers to Questions, Chapter VI:

(1) Should a pharmacist turn away prescriptions containing rare items which will probably not be called for again and which are destined to become "shelf warmers?" What percentage of prescriptions of this type call for official and specialty ingredients? (Pages 56, 57 and 58.)

It is of course desirable to keep the number of prescription items at a low figure. However, it is extremely difficult to do so and hardly compatible with professional service. In this connection one's attention is called to Table XXXV of the Report which shows that of 134 ingredients called for and not in stock, 88 or 65.7 per cent were specialties. They would have requested an investment of $90.26 or an average investment of $1039 or 3 cents more than the average price paid for prescriptions filled in the particular store in which this study was made.

(2) Are specialties introduced by many different manufacturers? (Page 58.)

A small number of manufacturers are responsible for a large proportion of the new specialties introduced.

(3) What is the prevailing form among specialties? (Pages 58 and 59.)

Only 30.4 per cent of recently introduced specialties are liquid, 21 per cent tablets, 13 per cent powder, 13 per cent ampuls, 7 per cent ointments, 6 per cent pills and 5 per cent capsules.

(4) Do new specialties usually enjoy a good sale? (Page 59.)

The introduction of new specialties does not necessarily mean that they will enjoy a large sale. Only 17.5 per cent of the specialties marketed in 1929, and 12.7 per cent of the specialties marketed in 1930 and 9.8 per cent of the specialties marketed in 1931 appeared in 35,000 prescriptions studied during the conduct of the National Drug Store Survey. It would thus appear that on an average only 13.4 per cent of the new proprietaries are prescribed to any extent.

(5) Are new proprietary specialties found in both professional and commerical type pharmacies? (Pages 59 to 61.)

New specialties are much more likely to be found in professional pharmacies than in the commercial type drug store. The manufacturer must therefore depend upon the professional pharmacy to a large extent when marketing a new product.

Answers to Questions, Chapter VII:

(1) Is there any information regarding the average content by weight or measure of proprietary specialties? (Pages 84 and 85.)

Paradoxically as it may seem, the smaller the size the specialty, the higher the cost. From the pharmacists' standpoint, this condition is unfortunate and frequently proves embarrassing in his relations to the patient who often complains at the cost—not being able to understand why such a small quantity of medicine can be so expensive.

I would like to state that along with many others, I share the opinion that many of the scientific proprietary specialty prescription products, particularly those of an organo-therapeutic and biological character are indispensable and deserving of unstinted praise and credit and represent a most valuable contribution to medicine. One must, however, pay equal tribute to official drugs and preparations and perhaps an appropriate end to this paper would be a quotation from the address of Reid Hunt, M.D., president of the United States Pharmacopœial Convention. At the May 13, 1930 meeting, Dr. Hunt said "The plant world will doubtless still yield valuable therapeutic agents; the possibilities of the animal world are by no means exhausted, but after all there is a limit to what can be expected from these sources. But the field of synthetic organic chemistry has no limits. Already some of our most valuable drugs have come from that field. The purpose of the "United States Pharmacopœial Convention is the promotion of medicine and pharmacy by selecting such materials as may be properly used as medicines and drugs. Therefore, any proved meritorious product, whether of vegetable or animal origin, or one of the many synthetic organic chemicals, the compounds of which run into hundreds of thousands, will in due course become 'official' and be admitted into the 'United States Pharmacopœia,' the oldest national pharmacopœia of a modern type in the world."

Is modern pharmacy's prescription compounding merely "pour out, count out, remove label, dispense original package?" I am not so sure about that. The National Drug Store Survey contradicts such a statement by pointing out that compounding prescriptions has not become a mere pouring out of a liquid or counting out a certain number of pills or tablets. In fact just the contrary is indicated. The survey shows that 65 per cent of the prescriptions calls for from two to ten ingredients.

AMERICAN DRUG MANUFACTURERS.

The officers for the ensuing year of American Drug Manufacturers are:

President, John F. Anderson, of E. R. Squibb & Sons, New Brunswick, N. J.

Vice-Presidents, S. DeWitt Clough, North Chicago, Ill.; Frederick S. Stearns, of Frederick Stearns & Co., Detroit; John G. Searle, of G. D. Searle & Co., Chicago.

Executive Vice-President, Carson P. Frailey, Washington.

Treasurer, Robert Lincoln McNeil, of McNeil Laboratories, Philadelphia.

General Counsel, Horace W. Bigelow, of Parke, Davis & Co., Detroit.

Additional Members of the Executive Committee, George W. Merck, of Merck & Co., Rahway, N. J.; Dr. A. W. Lesconier, of Parke, Davis & Co., Detroit; Dr. L. N. Upjohn, of the Upjohn Co., Kalamazoo, Mich.; John S. Zinsser, of Sharp & Dohme, Philadelphia; A. C. Boylston, of Mallinckrodt Chemical Works, St. Louis.

EDITORIAL NOTES

Members and Friends of the Scientific Section, American Pharmaceutical Association:

The 86th Annual Meeting will be held in Minneapolis, Minnesota, during the week of August 22nd.

The officers of the Scientific Section appreciate the interest you have shown in the past years, and are now making this appeal for your support to make the Minneapolis meeting a success. It is anticipated that a large number of papers will be submitted to the Section this year. The members, therefore, are requesting you to send in titles of papers at an early date.

In order to facilitate the presentation of papers, the officers have decided (at the suggestion of the Section) to arrange for a special Sub-Section to meet concurrently with the Second Session of the Scientific Section. The program of the Sub-Section will include all the papers dealing with Pharmacognosy. This is to be an experiment this year on which we can base our future plans.

Please note the following requirements of the Scientific Section:

1. The complete title and brief abstract, not to exceed 250 words, must be in the hands of the secretary in time for enclosure in the published program not later than July 15th. Please advise the secretary whether you will present the paper in person, also whether a lantern will be required for presentation.

2. Ten minutes shall be allowed for the reading of the paper. If the paper is too lengthy to be read in detail in this space of time it shall be presented in abstract. See the suggestion printed in the November 1937 JOURNAL.

3. In writing the paper the author should follow the procedure as outlined in the enclosed notice to contributors.

4. The by-laws provide that papers shall be presented in duplicate so that one copy will be available for publication and the other copy for the use of the Committee on Ebert Prize.

Our By-Laws also require that before publication all papers must be passed by the Board of Review of Papers. Authors can assist the Board of Review of Papers if, when writing the original paper they eliminate all non-essential material, presenting the subject in short, concise form.

DR. B. V. CHRISTENSEN,
Chairman, Scientific Section.

FRANCIS E. BIBBINS,
Secretary, Scientific Section,
5840 Washington Boulevard,
Indianapolis, Indiana.

SECOND PHARMACIST LIEUTENANTS.

The following candidates were nominated for appointment under an Act of Congress approved June 24, 1936, which limited appointments of officers in the Medical Administrative Corps to graduate pharmacists.

An examination will be held later to fill the remaining five vacancies and others that may occur in the meantime, of which due notice will be given, and it is important to fill the vacancies as they occur.

1—Leonard Paul Zagelow, Odessa, Wash., a graduate of the School of Pharmacy, State College of Washington, will be stationed at Fitzsimmons Hospital, Denver, Colo.

2—George Henry Wilson, Pittsburgh, Pa., a graduate of the College of Pharmacy, University of Pittsburgh, will be stationed at Carlisle Barracks, near Harrisburg, Pa.

3—James Wheeler McCormley, Wilson, Pa., a graduate of the School of Pharmacy, Duquesne University, will be stationed at Carlisle Barracks, near Harrisburg, Pa.

4—Ernest William Bye, Topeka, Kans., a graduate of the School of Pharmacy, University of Kansas, will be stationed at Fort Leavenworth, Kansas.

5—John Valdo Painter, a graduate of the College of Pharmacy, University of Minnesota, will be stationed at Fort Snelling, St. Paul, Minn.

Deeply interested in the health bulletins issued during the critical illness of **General John J. Pershing,** was **Charles W. Barnes,** prominent pharmacist in Valdosta, Ga., who served with the General from 1899 to 1903 during military operations against the Moros in Central Mindanao. He was a member of

the field hospital staff. In this campaign and through this type of work, Doctor Barnes and General Pershing formed a friendship which has continued through the years.

MINNESOTA'S PINES AND 10,000 LAKES.

This is the greeting of the Minnesota pharmacists who will come to Minneapolis. If you have not received an invitation to the meeting send for it. In Minnehaha the falls gleam and leap into the valley, and an hour brings you there from Minneapolis.

Minnesota druggists hope to make you come and extend a welcome. Dean Charles H. Rogers and his Committee have started the publicity.

Dean Wortley F. Rudd, of the Virginia Medical College, School of Pharmacy, has been honored by the State Dental Society by election as *honorary member* in recognition of his services.

Prof. H. W. Youngken, of the Massachusetts College of Pharmacy, Boston, Mass., is the *Grand Regent* of Kappa Psi Pharmaceutical Fraternity. Other officers inducted included C. E. Wilson, of Corinth, Miss., as *Grand Secretary-Treasurer;* and Dr. George Schicks, of the Rutgers College of Pharmacy, as *Grand Historian*.

The next convention of the fraternity will be held at Minneapolis, Minn., in connection again with the annual meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION.

COST OF MEDICAL STUDY.

The Senate Committee on Education and Labor has favorably reported to the Senate the resolution introduced by Senator Robert F. Wagner, of New York, calling for appointment of a special committee of Senators "to make a general study, investigation and analysis of the adequacy and cost of medical care in relation to income and ability to pay, and of ways and means to maintain and improve the health of the people of the United States."

The resolution would set up a committee of three Senators to make the study and would appropriate not to exceed $50,000 to cover the cost of making such a survey.

After being reported by the Education and Labor Committee the resolution was referred to the Committee for Audit and Control, which will pass upon the request for the $50,000.

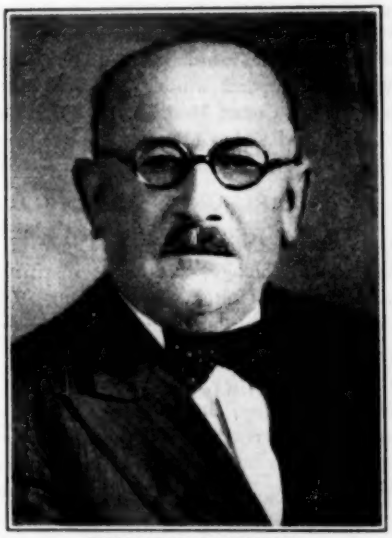
The proposed study is regarded as of interest to the whole drug trade because of the possibilities it carries for recommendations for socialization of medicine or for some system which will result in a wider distribution of medicines than is afforded at present.

THE BRITISH PHARMACOPŒIA 1941.

The annual report of the British Medical Association states that the coöperation of the Association has been sought by the British Pharmacopœia Commission in the preparation of the 1941 edition of the Pharmacopœia. Comments on various suggested deletions from and additions to the Pharmacopœia have been made to the Commission, with certain suggestions for increasing the usefulness of the publication.—From The *Pharmaceutical Journal* (April 30, 1938).

DEATH OF HENRY G. RUENZEL.

Henry G. Ruenzel, Honorary President of the A. PH. A., 1937–1938, and member of the State Board of Pharmacy of Wisconsin, for thirty-five years, until his retirement in 1937,



HENRY G. RUENZEL,
Honorary President, A. PH. A.

died April 2nd, aged seventy-seven years. He was a native of Milwaukee and a member of the first University of Wisconsin Pharmacy class, in 1885. A sketch of the deceased appears on page 783, in the September 1937, JOURNAL A. PH. A.

OBITUARY.

JOHN JACOB ABEL.

Dr. John Jacob Abel, internationally known pharmacologist and discoverer of adrenalin, died at Johns Hopkins Hospital, May 26th, after a brief illness, aged eighty-one years. He had been a member of Johns Hopkins faculty since 1893 and was made Professor Emeritus of Pharmacology and Director of the Laboratory for endocrine research in 1932, a position he held at his death.

Dr. Abel was born in Cleveland and graduated from the University of Michigan in 1883. He studied abroad and became famous for his discovery of adrenalin. He received many distinguished medal awards, and at the time of his death was preparing a series of papers on Tetanus. He was a son of George M. and Mary Becker Abel.

Dr. Abel was Lecturer and Professor of Materia Medica and Therapeutics at the University of Michigan; he was Honorary Member of the Philadelphia College of Pharmacy and Science; member of the Society for Biology, Buenos Aires. He perfected a method of synthesizing insulin so that it could be produced from other animal secretions. He received many medals, among them the Willard Gibbs Medal, Conné Medal, New York Chemists' Club, and Kober Medal.

DR. MORRIS CROWTHER HALL.

Dr. Morris Crowther Hall, Chief of the Division of Zoölogy, National Institute of Health, of the United States Public Health Service, died May 2nd, aged fifty-six years.

Dr. Hall's scientific activities led him into branches of zoölogy, and parasitology. In 1921 he discovered the value of carbon tetrachloride, in the treatment of hookworm disease. In 1936 he was made Chief of the Division of Zoölogy of the National Institute of Health. In this position he conducted and directed research work on pinworm infestation and trichinosis.

Dr. Hall was born in Golden, Colo., and educated at Colorado College and the University of Nebraska. From 1916 until his return to government service he engaged with Parke, Davis & Co., Detroit, Michigan, and was a lecturer at the Detroit College of Medicine. He also was a member of the International Health Board on the Rockefeller Foundation. He is a member of many scientific societies.

In 1906 he married Lola Davis, by whom he is survived; and also three daughters.

WILLIAM F. DOHMEN.

Wm. F. Dohmen, president of the F. Dohmen Co., wholesale druggists, Milwaukee, Wis., died May 10th. He was seventy-three years of age.

Mr. Dohmen graduated from the Philadelphia College of Pharmacy in 1884. After a year of European study he joined his father in the management of the F. Dohmen Co., becoming president of the firm in 1898. He was regularly at his desk in active charge of the business up to the last week before his death, and enjoyed the reputation of being one of the best informed drug men in the country.

He is survived by his wife and daughter, Marie, and by his nephews, Erwin and Fred Dohmen, who have been associated with him in the F. Dohmen Co. for the past twenty-five years.

HONORARY MEMBERSHIP OF THE BRITISH PHARMACEUTICAL SOCIETY.

At the present time there are thirty-five honorary and corresponding members of the Society. Of the former two are past members and three are present members of the Council who have been nominated by the Privy Council in accordance with the provisions of the Pharmacy and Poisons Act, 1933. The Society guards jealously the entrance to its membership, and in according honorary membership to the two distinguished individuals, Sin Humphry Rolleston and Professsor J. A. Gunn, who retired at the termination of their period of office in December last, it was bestowing upon them the highest honor which it was able to give. Of the remaining honorary and corresponding members nineteen are resident abroad. Two members, Professor H. H. Rusby and Professor Alexander Tschirch, enjoy the position of being both corresponding and honorary members of the Society; both are pharmacognosists, and both have been awarded the Flückiger medal for outstanding work on vegetable drugs.—*Pharmaceutical Journal* (British).

ANNUAL COLLEGE MEETING.

At the annual meeting of the members of the Philadelphia College of Pharmacy, March 28th, the following officers were reëlected:

President, Wilmer Krusen; *First Vice-President*, Ambrose Hunsberger; *Second Vice-President*, C. Mahlon Kline; *Treasurer*, Otto W. Osterlund; *Corresponding Secretary*, Theodore Campbell, Jr.; *Recording Secretary*, W. Wilson McNeary; *Curator of the Museum*, Arno Viehoever; *Librarian*, Ada S. Capwell; *Editor of the Journal*, Ivor Griffith.

Trustees: Henry Brown, Joseph Rosin, W. Wilson McNeary, Samuel P. Wetherill.

Committee on Publication: E. Fullerton Cook, J. W. Sturmer, Arno Viehoever, Mitchell Bernstein, Joseph K. Thum, Joseph W. E. Harrisson.

The ceremony of commemorating the retirement of Dr. Heizaburo Kondo from active university service upon the attainment of his age limit was held on the afternoon of April 11th, at the auditorium of the main hall of the Faculty of Medicine in the Tokyo Imperial University. The ceremony was held under the chairmanship of Dr. Ishihara, head of the Faculty of Medicine in the same university, and was attended by many prominent men including Dr. Kiroka Oguhi, one of the leaders of the Seiyukai party, and a pharmacist, as well as the students of the Tokyo Imperial University. Pharmacist-Lieutenant General Matajiro Watanabe who is a classmate of Dr. Kondo presided over the function.

MEDICAL ADVERTISING RESPONSIBILITIES.

It should be noted in this connection that the above exemption does not permit a drug vendor to escape the penalties of the act when advertising to physicians. If any false representations of material facts are made to the physician, the exemption would not appear applicable.

The provision of the new section 14 containing the criminal penalties for dissemination of false advertising relating to foods, drugs, devices and cosmetics becomes effective May 21, 1938, sixty days after the President approved the bill.

It will be seen that a number of different procedures and penalties are now provided for by the amended act. The commission may still follow its regular procedure looking toward a cease and desist order when the advertising involved is of a less serious nature, and where no intent to defraud is present and the respondent is honestly desirous of correcting any abuses.

In cases involving more serious misrepresentations the commission may, if it deems it in the public interest, apply for a temporary injunction.

In those cases where the use of the commodity may be injurious to health, or where there is an intent to defraud or mislead, procedure may be of criminal process punishable by imprisonment or fine or both. Such criminal proceedings will be conducted by the Department of Justice after presentation of all the facts by the commission to the Attorney-General.—*Oil, Paint and Drug Reporter.*

ANNUAL PHARMACEUTICAL CONFERENCE.

The officers of the U. S. P. attended the Annual Pharmaceutical Conference, May 16, 1938, at the Pittsburgh College of Pharmacy. There were present: Jerry McQuade, Charles Glen King, C. Leonard O'Connell, Edward C. Reif, George D. Beal, Walter A. Bastedo, Robert L. Swain, E. F. Kelly, S. L. Hilton, Solomon Solis Cohen, E. F. Cook, Julius A. Koch and others.

FORDHAM HONORS LATE DR. DINER.

At the Commencement exercises of the Alumni of Fordham University, to the student obtaining the highest average in all branches throughout his course, a memorial medal in honor of the late Dr. Jacob Diner will be presented. This will be an annual occasion.

Over five hundred physicians were given copies of the booklet "Revised Physicians' Pocket Manual of the U. S. P. and N. F. Preparations," published by the New York Pharmaceutical Association at the recent convention of the New York Medical Society. **Dr. J. Leon Lascoff** is chairman of the Committee.

OKLAHOMA OFFICERS.

O. L. Prather was elected president for the ensuing year. For the past three years, Mr. Prather has attended law school at the Tulsa law school, and will graduate in January 1939. He expects to take the bar examination in June 1939. A new Pharmacy Law for Okla-

homa will be one of the major objectives of his regime. Mr. Prather says that it is his purpose to carry on the fine work that Jess Stunkle has begun during the two years of his administration.

PERSONAL AND NEWS ITEMS.

Dr. Marston Taylor Bogert has been awarded the Priestley gold medal of the American Chemical Society. He has been a member of Columbia University faculty. In collaboration with students is the author of four hundred papers in the field of synthetic organic chemistry. He has received many medals and is a medalist of the Charles University in Prague. The gold medal will be formally awarded in Milwaukee at the American Chemical Society meeting.

Dr. Solomon D. Gershon received from the University of Illinois College of Pharmacy his degree of Pharmaceutical Chemist in June 1930, graduating with honors and receiving the Leo Mrazek Prize in Chemistry and also the P. A. Mandabach Memorial Life Membership award for high scholarship in Materia Medica. He also entered the competition for the Fairchild Scholarship award and passed this examination with a standing of 94 per cent and received the Scholarship in August 1930.

In September 1930 he came to the College as Assistant in Chemistry. He has held this position continuously since that time assisting in Organic, Synthetic, Quantitative and Qualitative Chemistry. In 1931 he passed the State Board of Pharmacy examination for Registered Pharmacist.

A testimonial dinner in honor of **Ivor Griffith** will be held on June 7th. Dean Griffith has succeeded former Dean LaWall.

Over 900 people packed the ballroom of the Pennsylvania Hotel, New York City, to pay tribute to Senator Jeremiah F. Twomey, Brooklyn pharmacist and chairman of the powerful Finance Committee of the New York State Senate, at the testimonial dinner given him by the New York Pharmaceutical Council. Seated at the speakers' table with the guest of honor were, left to right, Sen. A. Spencer Feld, co-author of New York's Fair Trade Law, Mrs. Feld, Senator Twomey, Mrs. Twomey and Sen. John J. Dunnigan, majority leader at Albany. Judge Harold Crawford, House sponsor, also attended.

Samuel S. Dworkin, New York, is compiling statistics concerning the lives of outstanding Jewish pharmacists and former pharmacists, now in other fields.

Any coöperation that your readers can extend will be greatly appreciated and will undoubtedly prove of value in the effort being made to establish a fact, the contribution of the Jewish Pharmacists, both past and present, to Pharmacy in general and as a citizen for the betterment of mankind.

If you have any information of any Jewish pharmacists, past or present, who are or were engaged in any other field such as medicine, dentistry, law, art, music, teaching, writing, banking, motion picture industry, politics, social service, philanthropy, etc., would you please communicate with me, joining with me as a collaborator in this work.—SAMUEL S. DWORKIN, 358 E. 204th St., Bronx, N. Y.

MEDICAL COST STUDY.

The Senate Committee on Education and Labor has favorably reported to the Senate the resolution introduced by Senator Robert F. Wagner, of New York, calling for appointment of a special committee of Senators "to make a general study, investigation and analysis of the adequacy and cost of medical care in relation to income and ability to pay, and of ways and means to maintain, and improve the health of the people of the United States."

The resolution would set up a committee of three Senators to make the study and would appropriate not to exceed $50,000 to cover the cost of making such a survey.

After being reported by the Education and Labor Committee the resolution was referred to the Committee for Audit and Control.

The proposed study is regarded as of interest to the whole drug trade because of the possibilities it carries for recommendations for socialization of medicine or for some system which will result in a wider distribution of medicines than is afforded at present.—*Drug Topics.*

MARIHUANA ACT.

The operations of the marihuana tax act thus far in the legitimate field have been at-

tended. A number of adjustments had to be made, but these were consummated with little inconvenience to the industry and to the government. Pharmacists and associations coöperated to the fullest extent with the treasury and narcotic officials.

PATENTS, TRADE-MARKS.

In largest part the report of the committee on patents and trade-marks, presented by Walton M. Wheeler, consisted of a comprehensive series of abstracts of material published in various records having to do with such protective measures and comprised virtually all Federal court decisions relating to patents, trade-marks and copyrights affecting the drug industry. One of the patent bills (H. R. 9259) is said to be part of the administration's attack on monopoly.

FORDHAM UNIVERSITY PUBLIC HEALTH COURSE.

Fordham University proposes a new course in public health for pharmacy students. New York: April 29, 1938. A gradual change in pharmaceutical curriculum throughout the United States, paving the way for the "Pharmacy of the Future," and aimed at the elimination of the present-day pharmacy with its heterogeneous collection of unrelated articles, was predicted last night by Dr. Leonard J. Piccoli of the Fordham University College of Pharmacy who announced plans for a new course in public health for pharmacy students at the "Better Health" meeting in the Bronx County Court House.

The new course is being prepared by a committee of outstanding public health authorities, headed by Dr. Piccoli, chairman, at the request of Pharmaceutical Syllabus Committee, representing the American Association of the Colleges of Pharmacy, the National Association of Boards of Pharmacy and the AMERICAN PHARMACEUTICAL ASSOCIATION.—From: Hamilton M. Wright, *Newspaper Syndicate Features.*

FAIR TRADE ORGANIZATION MEETING.

E. L. Newcomb, in an address, stated that wholesale druggists favored fair trade laws and believe that some organization representative of all lines of business should be created to sustain these laws and bring the public at large and all business to understand the results obtained when properly operating under them, extending eight substantial reasons. As they constitute one of the most effective trust barriers supplementing existing anti-monopoly laws and this is essential in order to afford more adequate and full protection to the end that fair prices may prevail for the consumer and the public at large than have heretofore ever been the case.

THE NARCOTIC INVENTORY.

It is necessary to file the Narcotic Inventory with application for registration before an inventory will be mailed. There will be no penalty if filed this month.

DRUG ACT ENFORCEMENT APPROPRIATION RAISED.

The Senate has passed the Department of Agriculture appropriation bill after increasing the appropriation for enforcement of the Food and Drugs Act by $150,000 and making a number of other changes in the bill as passed by the house.

The Senate struck out the house provision appropriating $1,000,000 for beginning work on four regional chemurgic research laboratories and instead allocated $100,000 to cover a survey to determine the location of these laboratories and the scope of the investigations to be made, and to coördinate their work with the research work already being done by the department.

Another amendment permits the naval stores conservation program to be conducted through the services of regional associations of producers instead of through county committees as in the case of other crops.

Other increases in appropriations made by the senate include the following—$9500 for study of investigations by the Bureau of Plant Industry; $30,000 for tung oil investigations and $7500 for the industrial utilization of farm products by the Bureau of Chemistry and Soils; $353,900 for various insect-control programs of the Bureau of Entomology and Plant Quarantine; $16,200 for cotton ginning investigations by the Bureau of Agricultural Engineering; $10,000 for cottonseed inspection, and $5000 for cottonseed market reports by the Bureau of Agricultural Economics.—*Oil, Paint and Drug Reporter.*

BOOK NOTICES.

The Chemistry of Plant Constituents, by OLE GISVOLD, Ph.D., and CHARLES H. ROGERS, D.Sc. Published by the Burgess Publishing Co., Minneapolis, Minn. Price, $3.50.

Advance in the Therapeutics of Antimony, by PROF. DR. HANS SCHMIDT and DR. F. M. PETER. Preface by Dr. Philip Manson-Bahr; ten diagrams. Published by George Thieme, Leipzig, Germany. Bound, $19.50; stitched, 18. R. M.

Drugs and Galenicals, by D. C. GARRATT. Published by John Wiley & Sons, Inc., 440 Fourth Ave., New York City. Price, $6.00.

Pharmaceutical Latin, by JACOB S. DORFMAN. Published by Lea & Febiger, Philadelphia, Pa. Price, $2.00.

A Brief Introduction to the Use of Beilstein's Handbuch der Organischen Chemie, by ERNEST HAMLIN HUNTRESS, Ph.D. Second edition, revised. Published by John Wiley & Sons, Inc. London: Chapman & Hall, Ltd. Price, $1.00.

Glandular Physiology and Therapy.—The book "Glandular Physiology and Therapy" was issued at the close of 1935. Although there has not been opportunity for the book to be revised since then, the sale still continued; 2095 copies were purchased in 1937.

"Useful Drugs.—This little book containing a selected list of drugs has always enjoyed wide acceptance. One reason for this is that it is used in many medical schools; the other is that the book is never out-of-date. Early in 1937 a thorough revision was made of the 1936 edition. At the close of 1937 the manuscript had almost been completed for an entirely new edition, which will be off the press in the spring of 1938. This is the first edition of 'Useful Drugs' in which the English name precedes the Latin name of the drug. The book is issued both in the regular pocket size and in an interleaved edition to meet the demand of teachers who desire their students to make notes alongside the text. The book not only is of service to teachers and students but is widely used as a reference guide by practicing physicians. The number of copies of 'Useful Drugs' sold in 1937 was 6495."—From *Jour. A. M. A.*, April 30, 1938.

Pharmaceutical Mathematics, by EDWARD SPEASE, Ph.C., B.S., Ph.M., Professor of Pharmacy, Dean of the School of Pharmacy, Western Reserve University and Directing Pharmacist, the University Hospitals of Cleveland. Second Edition. Publishers, McGraw-Hill Book Company, 330 West 42nd St., New York. Price, $1.75.

The general plan of the first edition has been followed; the chapters on manufacturing in quantity and percentage solutions have been rewritten; the chapters on profit and loss have been improved by a contribution made by Dr. L. H. Baldinger of the University of Notre Dame.

The book is intended as a textbook to be used in teaching the mathematics of pharmacy; the plan of instruction has been to assign a chapter or part of a chapter and to give such explanation of it as is necessary. Problems have been appended to each chapter.

Epitome of the U. S. Pharmacopœia and National Formulary.—The new Epitome was printed early in 1936. However, the policy of issuing interim supplements made it necessary to revise the Epitome in 1937. The demand for the book has been such that further printings must be made in 1938. The number of copies sold in 1937 totaled 8130.

GEORGIA SCHOOL OF PHARMACY.

A resolution has been addressed to Governor E. E. Rivers and University of Georgia officials to provide adequate quarters and equipment for the School of Pharmacy. The move is supported by the State Association.